Paid Circulation, 25,765

ANNUAL MEETING
May 19, 20, 21
Hotel Statler
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The New England Journal of Medicine

FORMERLY THE BOSTON MEDICAL AND SURGICAL JOURNAL — *Established 1828*

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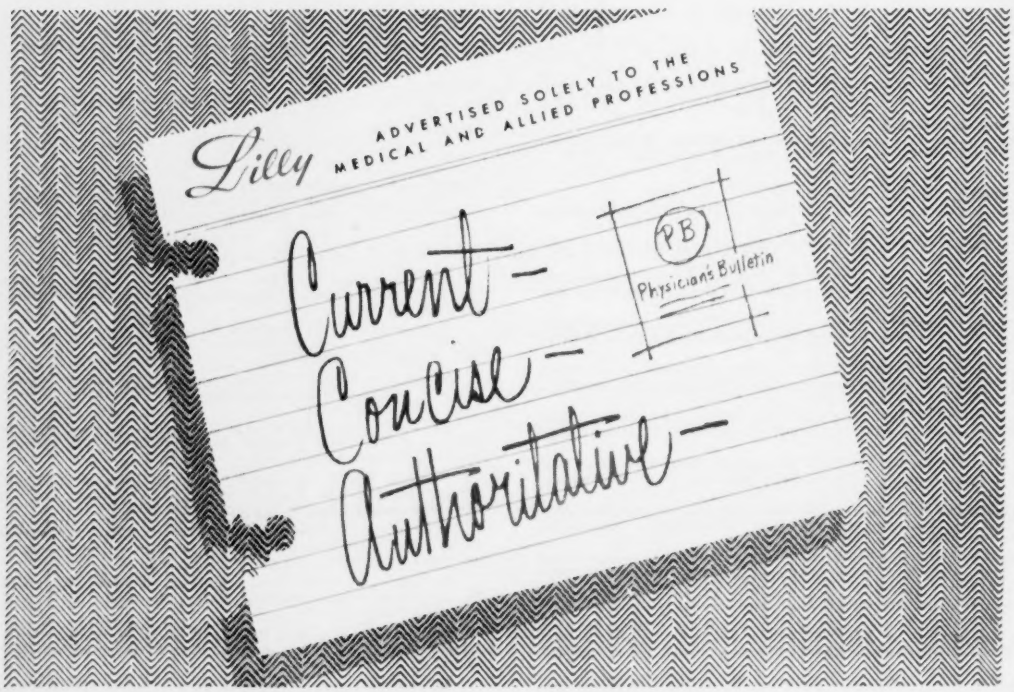
Entered as second-class matter, November 16, 1932, at the post office at Boston, Massachusetts, under the Act of March 3, 1879.
Published weekly at 8 Fenway, Boston 15. Domestic, $8.00 per year.



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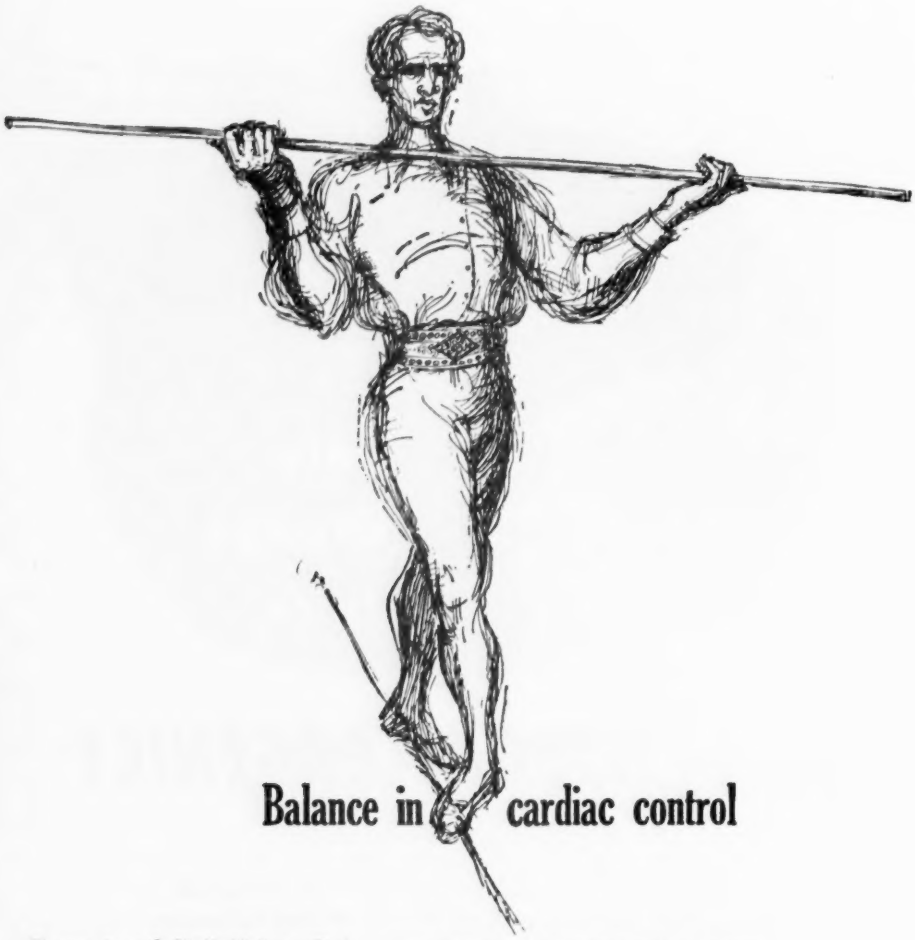

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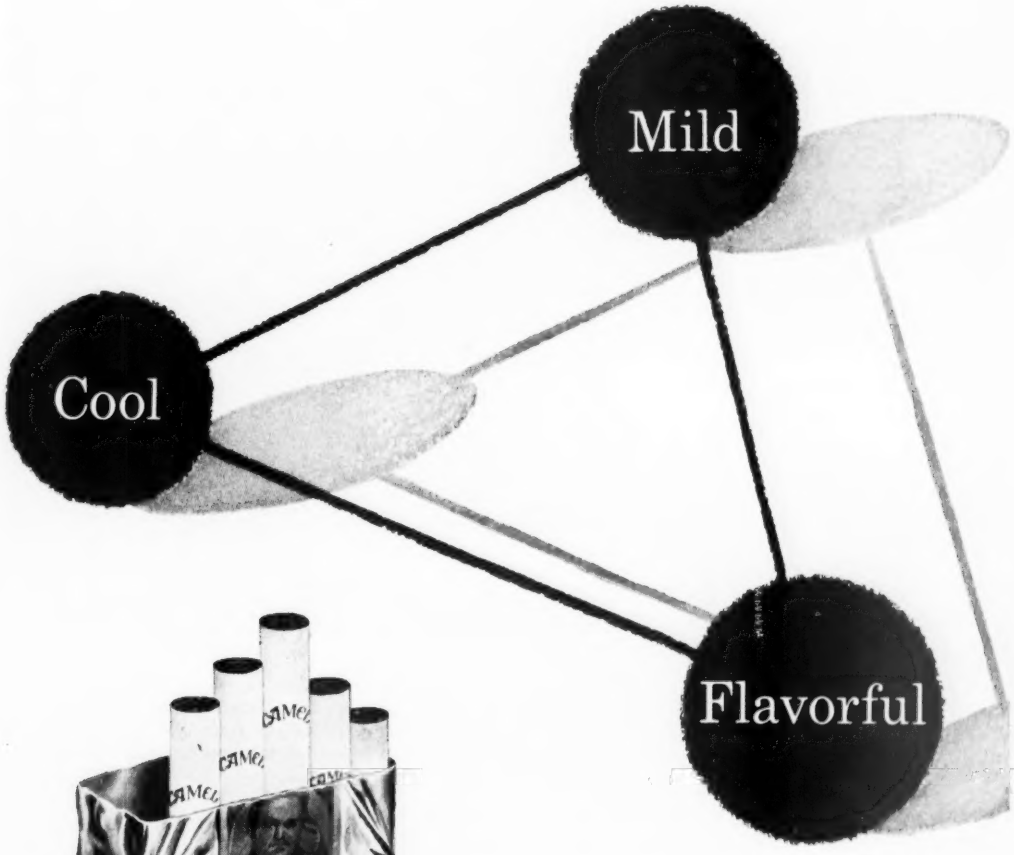

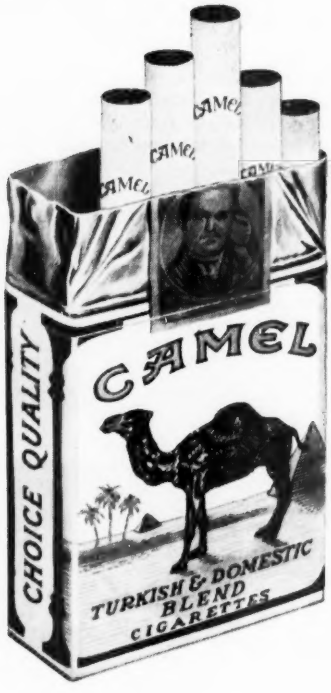

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THE USE OF TELEPAQUE IN CHOLECYSTOGRAPHY*

A Comparative Study

CLARK F. MILLER, M.D.,† AND JOHN W. CARRIER, M.D.‡

LEWISTON, MAINE

AMONG the relatively new orally administered radio-opaque mediums for cholecystography that are in common use today, Priodax (iodoalphionic acid) has enjoyed the greatest popularity since its introduction ten years ago. In recent years it has been in regular use at the Central Maine General Hospital. However, Menophen, placed on the market in 1944, is preferred by some workers. Both these mediums are satisfactory, but the trial last year in several institutions, and all reports agree that it is superior to previously used compounds, particularly in avoiding the disadvantages that might increase the probability of error in interpretation of the films.

The two most striking advantages of Telepaque are the denser shadow produced and the relative infrequency of side effects such as nausea and diarrhea. These two features may be more closely related to each other than is generally realized. Although Telepaque contains 15 per cent more iodine than Priodax (66.68 per cent as compared with 51.38 per cent) this difference in iodine content is not considered great enough to explain the better shadows obtained. Many of the poor shadows seen with Priodax are due to the accompanying diarrhea, which prevents adequate absorption of the dye from the intestinal tract. There is a definite correlation between the incidence of diarrhea and the occurrence of inadequately visualized gall bladders in cholecystography performed by oral administration of a compound, regardless of the medium used.

TABLE 1. *Results of Cholecystography with Priodax and with Telepaque.*

PATIENT	PRIODAX			TELEPAQUE			REMARKS
	SIDE EFFECTS	VISUALIZATION	INTERPRETATION	SIDE EFFECTS	VISUALIZATION	INTERPRETATION	
A. H.	None	Very poor	Gall-bladder disease	Diarrhea	Excellent	Normal	
T. K.	None	None	Gall-bladder disease	None	None	Gall-bladder disease	
D. K.	None	None	Gall-bladder disease	None	Poor	Gall-bladder disease	
M. T.	None	None	Gall-bladder disease	None	None	Gall-bladder disease	
F. M.	None	None	Gall-bladder disease	None	None	Gall-bladder disease	
A. G.	Diarrhea and vomiting	Very poor	?	None	Excellent	Normal	
C. R.*	None	Poor	?	None	Good	Stones	
L. T.	Diarrhea	Very poor	Gall-bladder disease	None	Very good	Normal	Patient very fat; 12 tablets Priodax; 6 tablets Telepaque.
G. R.	Diarrhea and vomiting	Fair	?	Diarrhea and vomiting	Good	Normal	Patient was having diarrhea and vomiting continuously
V. F.*	Diarrhea	Very poor	Gall-bladder disease	None	Excellent	Normal	
L. M.	Diarrhea	Poor	?	Diarrhea	Poor	?	
B. W.*	Diarrhea	Very poor	Possible stones	None	Good	Definite stones	No visualization on cholecystogram elsewhere
C. F.	Diarrhea	Poor	?	None	Excellent	Normal	

*Cholecystograms reproduced in Figures 1, 2 and 3.

In 1950 a new compound was introduced by Winthrop-Stearns under the trade name of Telepaque (3-[3-amino-2, 4, 6-triiodophenyl]-2-ethyl propanoic acid). It was given a fairly extensive

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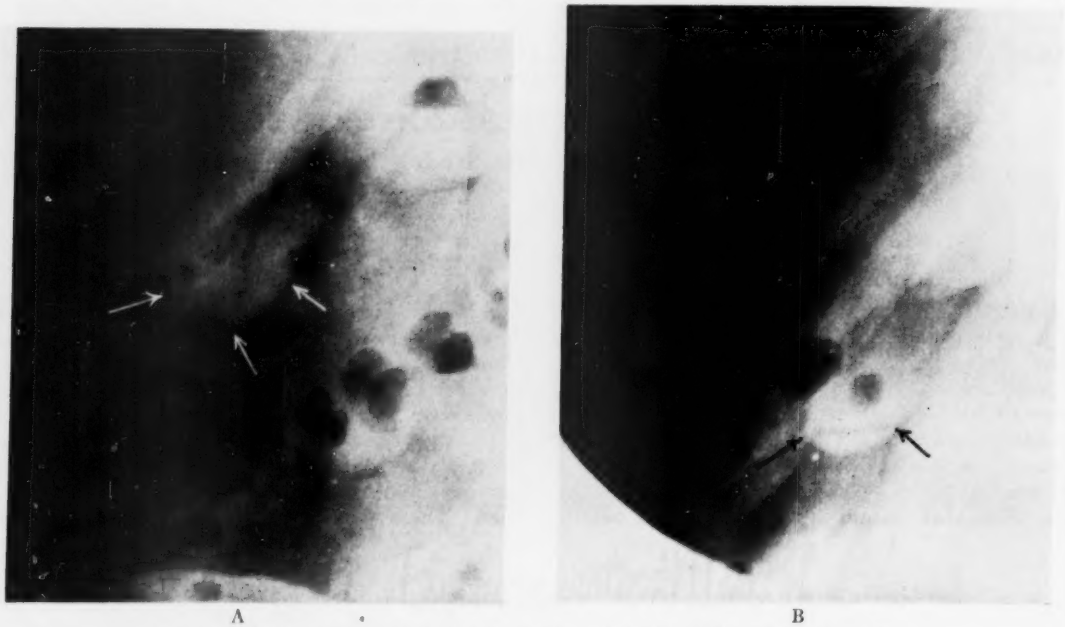
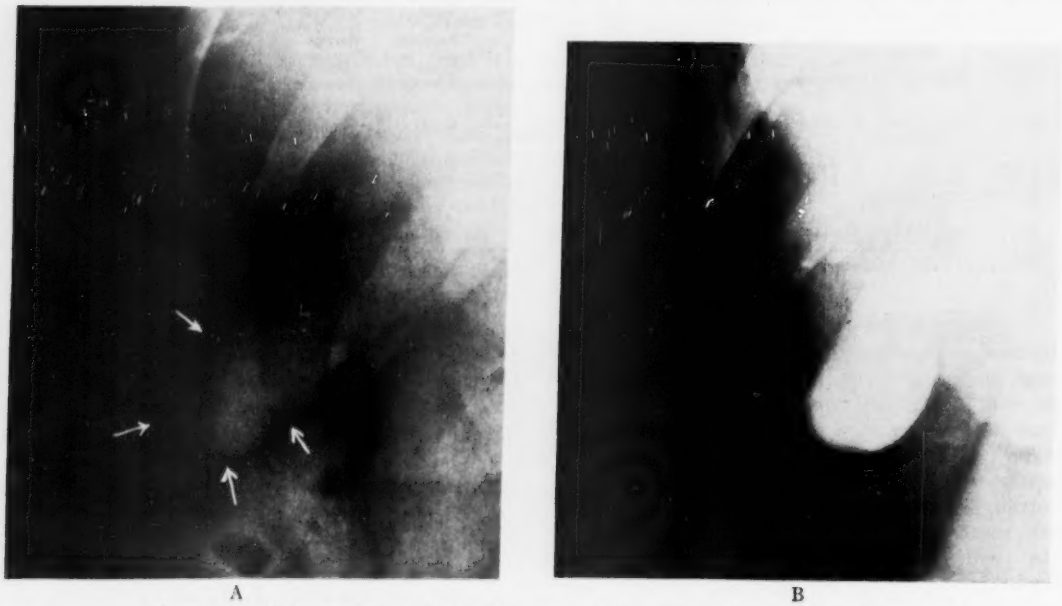
No detailed description of the pharmacology of Telepaque is attempted here. This information can be obtained from papers already published,[1] as well as from data obtainable from the Winthrop–Stearns Department of Medical Research. We are interested chiefly in drawing conclusions from the clinical experience that has already been accumulated in other centers and in this department.



A B

FIGURE 1. *Cholecystograms in Patient C. R. taken with Priodax (A) and Telepaque (B).*

At the Peter Bent Brigham Hospital the new compound was tried out on 50 unselected patients,[2] and a similar test series was reviewed at Washington University School of Medicine.[3] At New York Polyclinic Medical School and Hospital, 120 patients were given Telepaque, and comparison was made with 120 others examined at the same time with Priodax. In every study conducted in this way



A B

FIGURE 2. *Cholecystograms in Patient V. F. taken with Priodax (A) and Telepaque (B).*

the investigators have reported results that were superior to those obtained with Priodax.

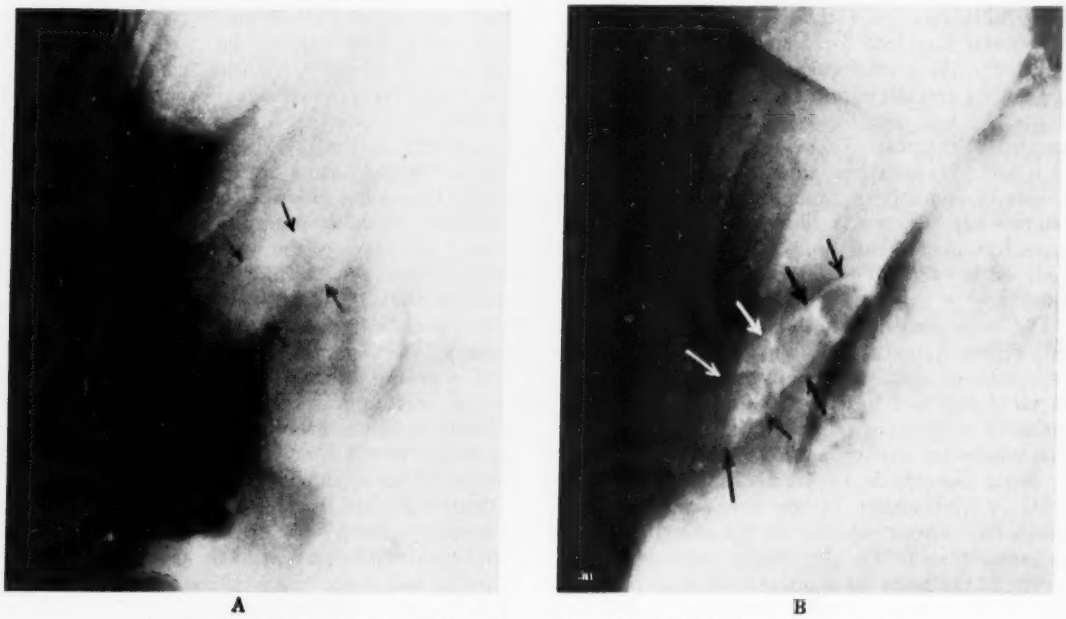
Although our own series is relatively small, we believe that it is of value for the very reason that the Telepaque was given to a small group of selected patients rather than to a large group of unselected ones. We continued to use Priodax on every patient in the usual manner, but whenever a case of nonvisualization came up, we repeated the examination within three days, using Telepaque. In this way, by comparison of the results with each medium on the same patient, the principles of accuracy in scientific investigation are adhered to as closely as is possible within the limitations imposed by any clinical study.

Two additional advantages of the new compound deserve mention. With Priodax it has been our practice to increase the dose by 50 per cent to 100 per cent in patients weighing more than 150 pounds. This has been found to be unnecessary with Telepaque, as was well demonstrated by a patient who weighed 275 pounds (L. T., in Table 1). Moreover, the tablets themselves are smaller and easier to swallow than Priodax tablets.

One possible disadvantage of Telepaque is its greater tendency to appear in the large bowel on the films. There is thus always the risk that the scattered radio-opaque material may obscure the gall bladder and present confusing shadows, but this is easily circumvented by the use of a sufficient variety of positions.

A great deal of emphasis has been placed on the increased frequency of visualization of the cystic and common ducts with Telepaque. We have not observed this in our series, but the number of cases has been too small for adequate judgment regarding this feature of the dye.

Of 13 selected cases (Table 1) in which cholecystograms failed to give adequate visualization of the gall bladder with Priodax and would therefore have been classified as demonstrating nonfunctioning gall bladders, 6 were considered normal after reexamination with Telepaque. Two other cases presented clear evidence of stones that could not be conclusively shown before because of the relative lack of density of the Priodax. In the remaining 5 cases, the examination with Telepaque presented essentially the same findings as those with Priodax. Thus, in more than half the cases in our series, the use of Telepaque enabled us to make a definite roentgenologic diagnosis when the findings after ingestion of Priodax had been either misleading or equivocal. Typical cholecystograms are shown in Figures 1, 2 and 3.



A B

FIGURE 3. *Cholecystograms in Patient B. W. Taken with Priodax (A) and Telepaque (B).*

SUMMARY AND CONCLUSIONS

A special study was conducted on a series of selected patients to determine whether the new cholecystographic compound Telepaque had sufficiently greater merit than Priodax to justify its

substitution in the routine examination of the gall bladder. The conclusion reached was that Telepaque is superior in three ways: in producing a denser shadow on the film; in causing fewer side effects; and in being more convenient for the patient to take.

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AN IMPROVED TEST FOR BILIRUBIN IN URINE*

GERALD KLATSKIN, M.D.,† AND LUITGARD BUNGARDS, M.D.‡

NEW HAVEN, CONNECTICUT

IN the development of new methods for detecting bilirubin in urine technical simplicity has generally been sacrificed for increased sensitivity and specificity. As a consequence many clinicians, for lack of time and laboratory facilities, have continued to use the less complicated, but relatively crude, methods of the past. There is still a need, therefore, for a test that combines simplicity of technic with maximum sensitivity and specificity. Notable progress has been made along these lines in recent years, but none of the simple methods devised have achieved the sensitivity of the more elaborate procedures.

The most sensitive methods depend on preliminary concentration of bilirubin, by adsorption on the precipitate of added calcium[1] or barium chloride,[2-4] or on talc,[5] followed by its oxidation[1, 4, 5] or diazotization[2, 3] to produce a characteristic color reaction. The controlled oxidation of bilirubin to biliverdin by ferric chloride in trichloracetic (Fouchet's reagent) or hydrochloric (Obermeyer's reagent) acid, which has proved superior to the older method of progressive oxidation by nitric acid or iodine,[6] serves as the basis for a number of sensitive methods.[4, 5] However, the color developed at low concentrations is often difficult to read, especially in the presence of other pigments and certain drugs. In attempts to overcome this difficulty and to increase sensitivity, methods based on the diazotization of bilirubin by various modifications of Ehrlich's diazo reagent have been devised. Several of these[2, 3] are among the most sensitive and highly specific tests available at present. Unfortunately, the instability of the diazo reagents usually employed, necessitating their fresh preparation before use, and the slow procedures of filtration and centrifugation involved in concentrating bilirubin in both the oxidation and diazotization technics have limited their widespread adoption in routine analyses.

Watson and Hawkinson[7] have effectively simplified the technic of concentrating bilirubin by employing a thick strip of filter paper impregnated with barium chloride. When this is dipped into urine momentarily, bilirubin is concentrated along the advancing front of urine drawn into the strip by capillary action. A similar method, in which urine is dropped onto a large plaster-of-Paris tablet containing barium chloride, has been described by Franklin.[8] In both procedures Fouchet's reagent is used to develop the characteristic blue-green color of biliverdin. As might be expected from the small amount of urine concentrated, these tests have proved less sensitive than those in which larger volumes of urine are used.

At a recent meeting of the American Chemical Society, Free and Free[9] described a new test for bilirubin in urine in which the simplicity of concentrating bilirubin on paper is combined with the sensitivity and specificity of a diazotization reaction, without the objectionable features of either. This is accomplished by the use of a special, bibulous cellulose-asbestos mat with an unusual affinity for bilirubin and capacity for its concentration, and by replacement of Ehrlich's reagent with a stable diazonium salt (p-nitrobenzene diazonium, p-toluene sulfonate) in the diazotization reaction. The latter reagent is incorporated in a tablet with sufficient sulfosalicylic acid to attain the optimal pH in the reaction mixture, sodium bicarbonate to facilitate solution of the tablet on addition of water, and boric acid as a diluent and binding agent. In performance of the test, 5 drops of urine are allowed to fall on the center of the special mat, thereby concentrating the bilirubin within a small circle on its surface. The reagent tablet is then placed on the moist mat and flooded with 2 drops of water, which are allowed to run down the sides of the tablet. The development of a purple or blue color in the area immediately surrounding the tablet within thirty seconds denotes the presence of bilirubin. According to the authors the test has been found to be highly specific and somewhat more sensitive than other commonly used methods.

Since this new test appeared to be unique in its simplicity and to offer some promise of being as

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Supported in part by a research grant (A47[C]) from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Public Health Service.

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accurate as more elaborate technics, an investigation of its sensitivity and specificity was undertaken. For comparative purposes a parallel study of three other urine bilirubin tests was carried out. The Sparkman method,[1] in which the bilirubin in a large volume of urine (25 cc.) is concentrated with the aid of calcium chloride and then oxidized with nitric acid, was chosen for its proved sensitivity in this laboratory, and the previously described Watson–Hawkinson[7] and Franklin[8] tests, based on adsorption of bilirubin on filter paper or plaster of Paris impregnated with barium chloride and oxidation with Fouchet's reagent, were selected because their simplicity approached that of the diazo mat procedures.

Methods

Consecutive urine specimens, sent to the laboratory for examination in connection with other liver-function studies, were tested for bile by two or more methods, as indicated below:

Sparkman + Watson–Hawkinson + Franklin	842
Sparkman + Watson–Hawkinson	24
Sparkman + Franklin	21
Sparkman + Free–Free diazo mat	500
Total	1387

The specimens were collected in the early morning, usually after an overnight fast, and analyzed within one or two hours. During this period no attempt was made to refrigerate the specimens or to protect them from the artificial light of the laboratory.

The technics were employed exactly as indicated by their respective authors[1, 7-9] except that the volume of urine and the amount of calcium chloride were cut in half to 25 cc. and 1 gm. respectively, in the Sparkman[1] method. The intensity of the color reactions obtained was graded from ± (trace) to ++++, and the absence of a characteristic color was recorded as 0. In the Watson—Hawkinson[7] strip test the color chart furnished by the authors was used in the grading. With few exceptions the Sparkman test[1] was performed by 1 technician, and all the others carried out on the same urine were performed independently by another. The 6 technicians who took part in the study were all well trained in the grading system used.

In a few tests the bilirubin content of the urine was estimated quantitatively by the diazo method of Golden and Snavely[10] and the oxidation method of Thoma and Kitzberger.[11]

Since the method of preparing the tablets and the mats required in the Free and Free[9] diazo mat test had not yet been described, it was necessary to obtain these from the laboratory that manufactures them under the direction of the Frees.* The tablets so obtained weighed approximately 140 mg. and measured 6 mm. in diameter and 3 mm. in thickness. The mats were provided in conveniently perforated sheets of 15 mats each, measuring approximately 2 cm. square and 3 mm. in thickness.

Parallel determinations of serum bilirubin, cephalin-cholesterol flocculation, thymol turbidity, alkaline phosphatase and, in most cases, bromsulfalein retention were carried out on simultaneously collected serum specimens in 1343 of the 1387 cases examined. In addition, a semiquantitative urobilinogen determination was carried out on all specimens of urine. Total and prompt-reacting ("one-minute") fractions of serum bilirubin were estimated by modifications[12] of the Malloy and Evelyn[13] and Ducci and Watson[14] procedures. The other methods have been described elsewhere.[15]

Results

Sensitivity

In a number of experiments icteric urine of known bilirubin content was diluted with water or normal urine, and tested for bilirubin by the four qualitative tests under investigation. The results of a typical experiment are presented in Table 1. It was found that the sensitivity of the diazo mat was consistently greater than that of the Sparkman, Watson–Hawkinson and Franklin methods. Although the Sparkman test approached the diazo mat in sensitivity, it required a hundred times the volume of urine, so that, in terms of absolute quantities of detectable bilirubin, it was actually far less sensitive. Thus, both methods were capable of detecting bilirubin in concentrations of approximately 0.05 mg. per 100 cc., but the diazo mat required only 0.125 microgm. of bilirubin for a positive reaction, whereas the Sparkman test required 12.5 microgm. This difference, however, had no great significance in the practical application of these tests, although the resultant small volume of

Table 1. *Comparative Sensitivity of Qualitative Tests for Bilirubin in Serial Dilutions of Icteric Urine in Water.**

Bilirubin Concentration	Diazo Mat Test	Sparkman Test	Watson–Hawkinson Test	Franklin Test
mg. per 100 cc.†				
5.82	++++	++++	++++	++++
2.91	++++	++++	+++	++
2.18	++++	++++	+++	++
1.46	++++	+++	++	++
1.09	+++	+++	++	+
0.73	+++	++	+	+
0.54	+++	++	+	+
0.36	++	++	+	±
0.27	++	+	±	±
0.18	+	+	±	0
0.09	+	±	±	0
0.06	±	±	0	0
0.05	±	0	0	0
0.03	0	0	0	0

*Essentially the same results were obtained in numerous other experiments in which icteric urines were diluted with either water or normal urine.

†Concentration of bilirubin determined by the diazo method of Golden and Snavely[10] in the original undiluted urine; all other values estimated from the dilution employed.

*We are indebted to Mr. Paul deHaen, of the Ames Company, Incorporated, Elkhart, Indiana, for a generous supply of this material, which at present is known as XA491 reagent tablets and mats, but is to be marketed in the future as "Ictotest," a registered trade-mark of the Ames Company, Incorporated.

urine required in the diazo mat method made it possible to eliminate both the slow procedure of filtration and the inconvenience of using volumetric glassware. These omissions were also a desirable feature of the Watson–Hawkinson and Franklin tests. However, in this instance they were achieved at the expense of sensitivity, as indicated by the fact that the lowest detectable concentration of bilirubin was 0.09 mg. per 100 cc. in the Watson–Hawkinson test and 0.27 mg. per 100 cc. in the Franklin test. Franklin,[8] using the Gibson method for quantitating bilirubin in urine, found that the barium tablet could detect concentrations down to 0.025 mg. per 100 cc. This discrepancy can probably be attributed to differences in the quantitative methods employed. In the present experiments, the bilirubin concentration was estimated by both the diazo method of Golden and Snavely[10] and the oxidation method of Thoma and Kitzberger.[11] The values obtained by the two procedures checked closely, and added bilirubin could be recovered quantitatively, suggesting that the results were reliable. Nevertheless, an attempt was made to check their validity by tests of the sensitivity of the diazo mat method in serial dilutions of icteric serum in urine, in water and in 5 per cent aqueous serum albumin. This was unsuccessful, since it was found that protein decreased the sensitivity of the test twofold to fivefold in direct proportion to its concentration, possibly by altering the pH of the reaction mixture or by carrying down bilirubin during its precipitation by acid. Similarly, there was a sixfold decrease in sensitivity in alcoholic dilutions of "pure" bilirubin* in chloroform, which could not be explained. Aqueous alkaline solutions of bilirubin were not tried because of their instability and unpredictable behavior during diazotization.[16]

A comparison of parallel routine urine analyses afforded the most convincing demonstration of the relative sensitivity of the four tests for bilirubin, and confirmed the results of the quantitative studies recorded above. This is demonstrated in Figure 1, in which it can be seen that the sensitivity of the diazo mat method was at least equal to, and possibly greater than, that of the Sparkman test, which was significantly more sensitive than either the Watson–Hawkinson or the Franklin procedure. Thus, in 500 urines tested by both the diazo mat and Sparkman methods, the results were identical in 461, whereas the diazo mat gave a stronger reaction in 34 specimens and a weaker reaction in 5. Moreover, in no case did the diazo mat fail to detect bilirubin when the Sparkman test was positive, although the reverse occurred in 13 specimens. In

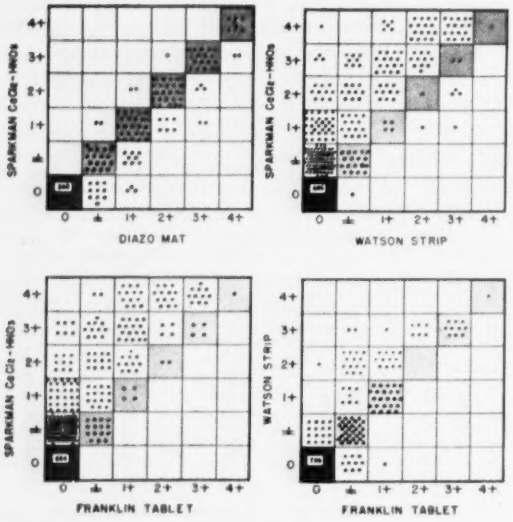

FIGURE 1. *Comparison of Parallel Tests for Bilirubin Carried out Simultaneously on the Same Urine Specimens.*
Cross-hatched areas indicate the number of specimens in which the concentrations of bilirubin demonstrated by both tests were identical. Figures in the solid blocks indicate the number of urines in which no bilirubin was demonstrated by either method.

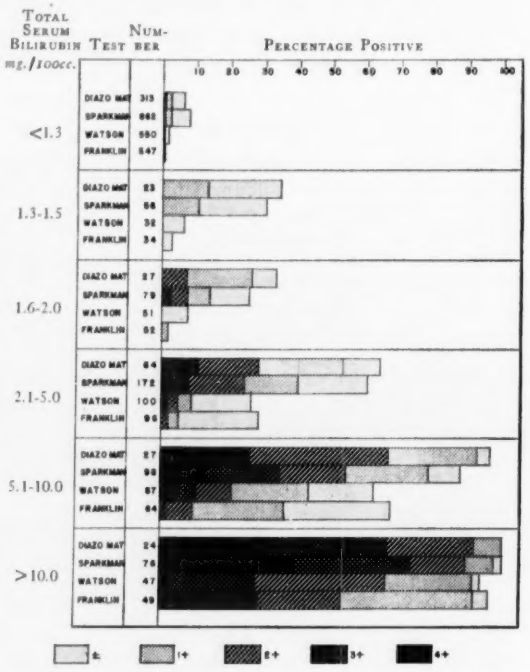

FIGURE 2. *Relation between the Total Serum Bilirubin Level and the Degree of Bilirubinuria Demonstrated by Several Tests. It should be noted that although there was considerable overlapping, as indicated in the section on methods, not all tests were carried out simultaneously on the same specimens.*

*Obtained from Hoffmann-LaRoche, Incorporated, Nutley, New Jersey.

contrast, the Sparkman test gave a stronger reaction than the Watson–Hawkinson barium strip in 228 out of 866 urines, and was positive in 120 urines that gave a negative reaction with the Watson–Hawkinson strip. In only 6 cases did the sensitivity of the barium strip exceed that of the Sparkman test. Similarly, the sensitivity of the Sparkman test greatly exceeded that of the Franklin barium tablet, as illustrated by the fact that the former gave a stronger reaction than the latter in 230 of 863 parallel tests, and was positive in 121 urines with a negative reaction by the latter method. Of the two less sensitive tests, the Watson–Hawkinson strip appeared to be superior to the Franklin tablet. Thus, of 842 parallel tests the strip gave a stronger reaction than the tablet in 59 and was positive in 17 urines with a negative tablet test. In 11 cases the tablet test gave a stronger reaction, but in none was it positive when the strip test was negative.

In Figures 2 and 3 the results of the urine tests are plotted against the concentration of bilirubin in simultaneously drawn serum to permit a more direct comparison of the four urine methods. Here again the diazo mat and Sparkman methods are seen to be more sensitive than the Watson–Hawkinson and Franklin tests, as indicated by the higher percentage of positive and more intense reactions at all levels of serum bilirubin.

A surprising number of urines showed no detectable bilirubin by any of the tests, despite significant elevations of the total serum bilirubin level (Fig. 2). That this was not due to differences in the partition of serum bilirubin into direct and indirect "fractions" is evident from Figure 3, which demonstrates a similar failure of bilirubinuria to appear at markedly elevated levels of direct-reacting serum bilirubin. Moreover, in the urines that contained bilirubin the amount was not always closely correlated with its concentration in the serum. These observations suggest that the level of serum bilirubin and its behavior in the van den Bergh reaction are not the only factors that determine the excretion of bilirubin in the urine. To be sure, the negative results obtained in some cases with the Watson–Hawkinson and Franklin tests merely reflected the insensitivity of these tests; however, with the diazo mat and Sparkman methods this does not appear to have been true. Rather, it must be assumed that bilirubin was either absent from the urine, or present in the undetectable, minute amounts thought by some[17] to occur in normal urine.

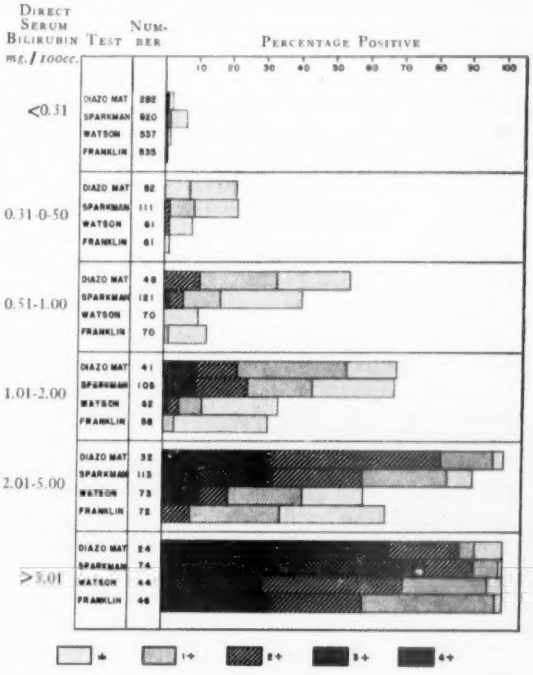

FIGURE 3. *Relation between the Prompt Direct (One-Minute) Serum Bilirubin Level and the Degree of Bilirubinuria Demonstrated by Several Tests.*

TABLE 2. *Estimate of the Probable Incidence of False-Positive Reactions Given by Qualitative Tests for Bilirubin in Urine.*

Test	Total No.	No. Positive with Normal Total Serum Bilirubin*	Confirmatory Evidence of Liver Disease†				Probable False-Positive Reactions	
			Clinical or Histologic	"Direct" Serum Bilirubin Increased‡	Other Urine Tests Positive	Total	No.	Percentage of Total
Diazo mat	478	20	15	14	9	18	2	0.4
Sparkman	1343	69	40	11	25	42	27	2.0
Watson–Hawkinson	847	9	4	2	9	9	0	0
Franklin	842	3	1	1	3	3	0	0

*Less than 1.3 mg. per 100 cc.
†Many of the cases fell into more than one category, which accounts for the apparent discrepancy in the totals listed.
‡Greater than 0.3 mg. per 100 cc.

Specificity

Since bilirubin often appears in the urine when there is hyperbilirubinemia, and may occasionally do so in its absence in some types of liver disease,[18] the only false-positive tests for urine bilirubin that

can be recognized with certainty are those that occur in persons without evident liver disease or hyperbilirubinemia. For that reason, in appraising the relative specificity of the methods under consideration, the incidence of false-positive tests was estimated from the number of positive reactions in persons with normal serum bilirubin concentrations in whom hepatic damage could be excluded. When there was unequivocal clinical or histologic evidence of liver disease, or an increase in the direct-reacting "fraction" of serum bilirubin or confirmation of a positive test for bilirubinuria by more than one method, it was assumed that the results of the test were valid.

There were only 2 false-positive reactions in the 478 diazo mat tests carried out, an incidence of 0.4 per cent (Table 2). One of these was a + reaction in a patient with rheumatoid arthritis, hepatomegaly and minor alterations in liver function, and the other a ± reaction in a patient with carcinoma of the esophagus suspected of having hepatic metastases. Conceivably, focal hepatic lesions were present in both, but needle biopsy of the liver failed to disclose any abnormalities in the former, and tests of liver function were normal in the latter, in whom, unfortunately, no biopsy was available.

The Sparkman test appeared to be less specific than the diazo mat, in that it gave rise to 27 false-positive reactions in a total of 1343 tests, an incidence of 2 per cent (Table 2). In all but 2 cases these were graded as a trace, and may have represented errors in interpretation rather than reactions to interfering substances. In contrast to the diazo mat test, in which there was never any difficulty in recognizing the characteristic color reaction of bilirubin, it was often difficult in the Sparkman test to distinguish between the slight discoloration of the normal urinary pigments produced by concentrated nitric acid and the color reaction of traces of bilirubin.

No false-positive reactions were encountered in any of the tests carried out by the Watson–Hawkinson and Franklin methods (Table 2), indicating a greater degree of specificity than either the diazo mat or the Sparkman procedure.

The authors of the diazo mat method[9] indicated that the characteristic blue-purple color reaction of bilirubin occurred within thirty seconds. In the present study it was found that, although the maximum color developed within that interval, it showed no tendency to fade over a considerable period and there were no delayed color reactions from interfering substances, so that precise timing did not appear to be essential. However, it was observed that even traces of albumin produced a pink color. Fortunately, this was readily distinguished from that produced by bilirubin. As indicated above, however, albumin reduced the intensity of the color at all concentrations of bilirubin and reduced the sensitivity of the test.

Stability of Urinary Bilirubin

The instability of bilirubin in urine is well known,[19] and may be of importance in the practical application of tests for bilirubinuria. For that reason, the effects of urine storage, refrigeration and exposure to light were investigated. It was found that, under refrigeration for periods up to sixteen hours, urine showed no significant decrease in bilirubin by any of the methods tested. However, when urine was exposed to room temperature, there was a progressive loss of detectable bilirubin, which affected the results of the diazo mat test more seriously than any of the oxidative methods. No doubt this was related to the conversion of bilirubin to biliverdin, which does not react with diazonium compounds. Exposure to light did not appear to affect the results of any of the tests, provided the specimen was refrigerated.

Discussions

From the data presented it is clearly evident that the diazo mat method of Free and Free[9] is a highly sensitive and specific test for bilirubin in urine. Although the Sparkman[1] test approaches it in sensitivity, it is less specific, takes more time and requires equipment that renders it impractical for mass testing or for bedside use. As far as simplicity and speed are concerned, the Watson–Hawkinson[7] and Franklin[8] methods are the equal of the diazo mat, but are far less sensitive. Moreover, they both require a liquid reagent, which is somewhat less convenient for transportation by the practicing physician than the tablets used in the diazo mat method.

The greater sensitivity of the diazo mat test to losses of bilirubin due to storage of urine at room temperature appears to be a disadvantage. However, from a practical point of view it was found that such storage for periods up to two hours did not materially affect the results of the test.

Although it was shown that the diazo mat test was more sensitive that the other three methods investigated, the inordinate number of negative results obtained in subjects with significantly elevated total and "direct" serum bilirubin levels, 35 and 39 per cent respectively, raises the question of whether the sensitivity of the test is sufficiently great to warrant its general adoption, or whether other tests, for which much greater sensitivity has been reported,[3-5] should be used more widely, even though they are more difficult to perform. Obviously, it would be desirable to use a test that detected bilirubin in urine whenever the serum bilirubin was increased. However, if its sensitivity was so great that it gave a positive reaction in normal urines, as in Naumann's[5] test, it would lose much of its value as a diagnostic test. The Harrison[4] test, on the

other hand, was found to be more specific, and to be capable of detecting concentrations of bilirubin down to 0.003 mg. per 100 cc. of urine,[8] a value much lower than the 0.05 mg. found for the diazo mat in the present study. However, the quantitative method employed by Godfried[8] differed from that used in this laboratory, and when the sensitivity of the Harrison test was checked by the diazo method of Golden and Snavely,[10] it was found to be exactly the same as that of the diazo mat test, so that the latter, which has the advantage of simplicity and speed is to be preferred. Moreover, the number of positive reactions that the diazo mat gave in subjects with liver disease and normal serum bilirubin levels suggests that the test is capable of detecting any significant increase in bilirubin excretion, and that there would be no advantage in increasing its sensitivity.

Summary

The diazo mat test for detecting bilirubin in urine suggested by Free and Free was investigated and found to be unique in its simplicity, sensitivity and specificity. The method depends on concentrating bilirubin on a special, bibulous cellulose-asbestos mat and diazotizing it with a stable diazonium compound incorporated in a tablet. It was capable of detecting concentrations of bilirubin as low as 0.05 mg. per 100 cc. of urine, and proved to be more sensitive than three other widely used methods that were investigated, and more specific than the most sensitive of these.

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CHEMOTHERAPY OF TUBERCULOSIS*

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Many substances have been used in the treatment of tuberculosis with the supposition that the resistance of the patient to the disease might be enhanced. Of these, gold salts and tuberculin were the most widely employed. A direct effect on the tubercle bacillus was not even hoped for in most cases. A direct effect of the sulfone and sulfonamide derivatives (Diasone, Promine and Promizole) was expected but was probably seldom attained.

The era of effective chemotherapy began with the discovery of the action of streptomycin against the tubercle bacillus in 1944 and 1945.[1,2] Several extensive co-operative studies, begun in 1946, led to the conclusion in the next few years that streptomycin was useful in the treatment of tuberculosis, but that its effect was limited, when used alone, by the development of organisms resistant to streptomycin in 80 per cent of patients whose sputums remained positive after four months of treatment. Although creating a serious problem when 2 gm. or more was given daily, renal and eighth-cranial-nerve toxicity was reduced to a reasonably satisfactory low incidence and lack of severity when the daily dose was reduced to 1 gm. daily; it became still less if 1 gm. was given twice a week. Therapeutic effectiveness continued to be quite satisfactory at this lower dosage.

The combination of PAS (paraminosalicylic acid) with streptomycin was begun in this country in 1948.[3] A trial of many different dosage combinations, in several thousand patients, led to the conclusion that 1 gm. of streptomycin twice weekly, given intramuscularly, and 12 gm. of PAS daily, given by mouth, was as effective a regimen as any. It was accompanied by negligible toxicity and a great reduction in the rate of the emergence of streptomycin-resistant organisms. This now oc-

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Presented at the 11th Annual Session of the New England Postgraduate Assembly, Boston, Massachusetts, October 28, 1952, and solicited by the Editor.

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curred in about 15 per cent of patients with positive sputums at the end of four months of treatment. Presumably, the optimum dose of PAS, when used with streptomycin, is 10 to 12 gm. daily. Whether or not a smaller daily dose might be just as effective is not certain, but the prevailing clinical impression is that it may not be. An intermittent schedule of both 1 gm. of streptomycin and 12 gm. of PAS twice weekly has been found to be less effective than a combination of 1 gm. of streptomycin given twice weekly and 12 gm. of PAS given daily.[4]

This lessened development of resistant organisms has permitted longer-term therapy, with continuing beneficial effects. It is thought at present that four months of therapy are rarely sufficient and that almost all patients should be treated for at least eight months. Most patients with relatively advanced disease should receive treatment for a year, and many with far-advanced disease for one and a half to two years.

It has become customary in the evaluation of chemotherapeutic agents to grade the change in serial x-ray films as "marked," "moderate" and "slight" degrees of improvement, "no change" and "worse." When patients received their first course of combined treatment with streptomycin and PAS moderate or marked improvement occurred in 50 per cent, slight improvement, or no change, in 40 per cent and worsening in 10 per cent, after four months of therapy. The number showing moderate or marked improvement rose to 70 per cent after eight months of treatment and to 80 per cent after a year's treatment.[5, 6] It must be stressed that these results refer to patients who received continuous chemotherapy without interruption and that this was their first course of treatment. Equally good results have not been found when treatment was interrupted.

The effect on the bacillary content of sputum of patients treated with streptomycin and PAS was immediate and marked in most patients receiving their first course of treatment. Frequently, negative smears and cultures for tubercle bacilli were obtained almost immediately, even though a large cavity was still seen in the x-ray film. This was only a temporary inhibition and could not be taken as a sign that the goal of treatment had been reached, since the sputum again became positive when treatment was stopped prematurely. A puzzling phenomenon was found occasionally in cases treated for a year or more in that the sputum remained negative for over a year after treatment was stopped, in spite of the fact that what seemed to be a cavity was still seen in the x-ray film. Unfortunately, such cases have been the exception rather than the rule, and ordinarily the sputum became positive again soon after chemotherapy was stopped, when a definite cavity was still visible in the roentgenogram. It was noted that blocked cavities or nodules, removed surgically, contained many tubercle bacilli when their contents were examined by smear, but that the bacilli from these lesions did not grow by any cultural methods thus far applied. Whether these organisms were really dead or had only lost their power to reproduce temporarily is not clear. It is evident that all lesions were not sterilized, since viable tubercle bacilli have been recovered from the sputum of some of these patients after operation. This situation has not been found in open cavities in resected specimens. Tubercle bacilli from these lesions usually have grown readily on culture mediums.[6]

The clinical effectiveness of PAS, when used alone, has been found to be slight. In general, it is thought best to use it in combination with streptomycin.

Amithiozone was introduced into this country in 1949, after extensive trial in several European countries. The recommended dosage has been 100 to 200 mg. a day. Used alone, it has a low order of therapeutic effectiveness and clinically has not seemed to enhance the effects of streptomycin given concurrently. Toxic effects were varied and occasionally severe, consisting of nausea, vomiting, evidence of liver or kidney damage, anemia and leukopenia and occurring singly or in combination in the same patient. These effects were usually reversible when the drug was stopped promptly. At present, amithiozone is usually reserved for patients who are considered to be in great need of chemotherapy and in whom, for one reason or another, the use of other agents is not feasible.

Neomycin, although quite active against the tubercle bacillus in vitro and in vivo, has thus far proved to be too toxic for general use in the treatment of tuberculosis. A high incidence of deafness and renal disturbance has occurred in the patients treated.[7]

Viomycin has been found to have a high degree of activity against the tubercle bacillus in the test tube and in animals.[8, 9] The available data indicate that it is at least moderately effective clinically. When a daily dosage of approximately 2 gm. was used, renal and auditory toxic effects similar to and more marked than those of streptomycin occurred. In addition, there were fairly marked changes in the serum electrolytes consisting of hypokaliemia, hypocalcemia, hypophosphatemia and hypochloremia, as well as an increase in the carbon dioxide combining power.[10] However, it was found that toxic effects diminished when a lower dosage was employed, and recent data showed that when 1 or 2 gm. was given twice weekly, by intramuscular injection, the drug could be used for considerable periods without troublesome toxicity. Thus, whereas the clinical effectiveness of viomycin may be somewhat less than that of streptomycin, it is at present believed to be a useful drug for

certain patients when other chemotherapeutic agents are contraindicated.[11]

Although, when given alone, terramycin has little clinical effect it has been found to be similar to PAS, when given in combination with streptomycin, in diminishing the emergence of streptomycin-resistant tubercle bacilli.[6] A dosage of 5 gm. of terramycin daily by mouth and 1 gm. of streptomycin intramuscularly twice a week was used. Since such a dosage of terramycin was costly and often was maintained with difficulty, the effectiveness of lower doses is now being explored.

Aureomycin, when given alone in a dosage of 3 gm. daily, seemed to have no effect on the course of pulmonary or laryngeal tuberculosis. Evidence of effect was also lacking on tuberculous sinuses.[12] It was not used in combination with streptomycin.

Recently, a new series of chemotherapeutic agents related chemically to nicotinic acid has been studied. The results of a clinical trial of pyrazinamide (aldinamide) were the first to be announced.[13,14] With a daily dosage of 2.8 gm. for six weeks, immediate and marked symptomatic improvement occurred. Roentgenographic evidence of improvement was reasonably satisfactory, considering the short duration of treatment. There was generally no evidence of toxicity. However, pyrazinamide-resistant tubercle bacilli were found in the sputum of a large proportion of patients within a few weeks, and clinical experience has confirmed the fact that the period of effectiveness of pyrazinamide, when used alone, is often short. Also, 12 gm. of PAS given daily in combination with pyrazinamide failed to delay the emergence of pyrazinamide-resistant organisms. A study of the use of pyrazinamide, 3 gm. daily, and isoniazid, 150 to 300 mg. daily, is being undertaken at present. All that can be reported is that toxicity has not been troublesome and clinical results have been reasonably satisfactory. There has not been enough time to determine, by clinical impressions or laboratory methods, whether or not the emergence of organisms resistant to either drug has been delayed.

Recently, the clinical studies of isonicotinic acid hydrazid (isoniazid) and its isopropyl derivatives have been published.[15,16] Its effectiveness in the treatment of miliary and meningeal tuberculosis has been found to be quite marked.[17] Isoniazid was given in a dosage of 150 mg. daily by mouth to 88 patients at this hospital, a large proportion of whom were suffering from relatively chronic disease. The previously reported favorable effect on symptoms was confirmed. At the end of four months' treatment, only 12 per cent of patients showed moderate, or marked, improvement in serial roentgenograms. When only patients whose x-ray films demonstrated a good deal of exudative disease were considered, 33 per cent had moderate or marked improvement. Twenty-two per cent gave x-ray evidence of worsening at the end of four months. In 50 per cent organisms resistant to 5 microgm. per cubic centimeter, or more, of isoniazid were recovered from the sputum at the end of four months. This was regarded as a significant degree of bacterial resistance, since blood levels ordinarily were not higher than 3 or 4 microgm. per cubic centimeter. This impression is also borne out by the fact that the patients who showed x-ray worsening were confined to the group whose organisms had become resistant to this degree. It was concluded that isoniazid, when given alone in a daily dosage of 150 mg., is not as effective as streptomycin and PAS in the treatment of pulmonary tuberculosis. Preliminary data indicate that this is also true when isoniazid is given in a daily dosage of 300 mg.

Toxic reactions to isoniazid have included severe allergic reactions, hyper-reflexia, convulsions, constipation, difficult micturition, undue sensitivity to adrenergic drugs and atropine, sudden drops in blood pressure, postural vertigo, eosinophilia and a decrease in hemoglobin. Experience has shown that these toxic manifestations were rarely serious enough to make it necessary to stop treatment and frequently disappeared spontaneously while treatment was continued. The one exception consisted of severe allergic reactions, which, although rare, were sufficiently severe to make it necessary to stop treatment altogether.

At present, combined therapy, in which isoniazid is used with PAS and with streptomycin, is being compared with results obtained with streptomycin and PAS. Up to the present time there have been no undue toxic manifestations. As yet, there are insufficient clinical data to determine whether or not these combinations may prove to be superior to or even equal to streptomycin and PAS, from the point of view of either clinical response or delay of the emergence of organisms resistant to the various drugs. Since long-term chemotherapy has been found to be vital in the treatment of tuberculosis, prevention of the development of resistant tubercle bacilli is an important measure of the success of any regimen. Because this measure is unknown at present in any of the isoniazid combinations, it is believed that a regimen of 1 or 1.5 gm. of streptomycin daily, or 1 gm. twice weekly, with 12 gm. of PAS given daily in any case, is preferable for practical purposes in the treatment of patients suffering from pulmonary tuberculosis who have not had previous chemotherapy.

In all the attention now being paid to chemotherapy, it should not be forgotten that bed rest is just as necessary as ever in the treatment of tuberculosis. All forms of collapse therapy are still useful in suitable cases. Whereas chemotherapy has not shortened the duration of hospital stay, it has helped the recovery of many patients who would otherwise have succumbed. The lives of many additional patients have been prolonged indefinitely, although the disease was not arrested.

Also, chemotherapy, when given for a fairly long time, has made possible the successful surgical excision of the greater part of the remaining lesions in the small proportion of patients suitable for this procedure.

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CORRECTION OF RECTAL PROCIDENTIA

The Thiersch Operation as a Simple Palliative Procedure

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PROCIDENTIA of the rectum is defined as the "abnormal descent of all the coats of the rectum with or without protrusion through the anal orifice." This paper is concerned with the condition in the elderly patient primarily and with the type of procidentia that protrudes through the anus as a large mass in the intergluteal region.

Weakness in the musculofascial supports of the pelvic floor and the added factor of increased intra-abdominal pressure from any cause constitute the main elements in the etiology of rectal procidentia. This is manifested by invagination of the pelvic peritoneum into the anterior rectal wall, with subsequent protrusion through the anal orifice. The rectum appears in the intergluteal region as a bright red mass covered by a mucous membrane that is grooved with circular folds. The mucous surface may reveal numerous erosions, bleeding and accumulations of pooled mucus. At first the procidentia appears only with severe straining and reduces itself spontaneously; as the condition continues to recur it may appear on the slightest effort and require manual reduction. Atonicity of the anal sphincter and incontinence are sequelae. The patient complains of pressure sensations, backache, constipation, poor bowel control, bleeding and constant fatigue.

The immediate treatment of rectal procidentia requires reduction of the mass to its former position within the pelvis. With the patient in recumbent position the gloved index finger covered with dry gauze is inserted into the opening to the bulging rectum. The gauze forms a firm attachment to the mucous membrane and prevents slipping of the finger. Firm inward pressure is applied and the mass gradually replaced. If there is edema of the extruded tissues it may be necessary to perform the reduction under a general anesthetic. The most difficult problem in management is to prevent recurrences with subsequent chronic invalidism.

Innumerable operative technics have been employed in an attempt to cure this hernia-like abnormality. Successful results are attained frequently in young, healthy persons who have strong tissues amenable to repair. However, the elderly patient with weakened musculofascial tissues, inefficient circulation and poor nutritional status is no candidate for extensive surgery. It is in this type of case that the Thiersch operation is of greatest usefulness.

First described by Thiersch in 1891 at the Congrès des naturalistes et médecins allemands à Halle, the procedure is designed to diminish the size of the anal canal by means of a nonyielding wire cuff. A mechanical barrier to the prolapsing mass of tissue is thus obtained. With the patient in lithotomy position 1 per cent novocain is infiltrated into the anterior and posterior portions of the perianal tissues. Small vertical incisions are made in these areas through the skin and subcutaneous tissues. A nonpliable 13-gauge or 15-gauge needle inserted through the posterior incision is directed at first laterally and then anteriorly, encircling the anal musculature on the right side and emerging through

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the anterior incision. A second needle is similarly inserted on the left side. With these two needles placed parallel to each other, No. 22 stainless-steel wire is threaded through the beveled ends, appearing in the posterior wound (Fig. 1). The needles are

FIGURE 1. *Heavy Needles Inserted into the Postanal Wound and Encircling the Anal Musculature in the Direction of the Broken Arrows.*
Wire has been threaded through the needles.

removed, and the wire tightened about the index finger of the surgeon (Fig. 2). The skin incisions are closed.

There is little postoperative pain. Hot boric compresses or hot sitz baths offer satisfactory relief from discomfort. The patient may be ambulatory at once. Antibiotics for seventy-two hours are advised to counteract wound infection. A daily enema is required indefinitely to prevent fecal impaction.

CASE REPORTS

CASE 1. N. P., a 75-year-old woman, was admitted to the hospital on March 8, 1952, with the complaint of rectal protrusion of 20 years' duration. This protrusion had become progressively larger, and during the past 10 years had reached "the size of a grapefruit." At first returning spontaneously, the mass now required manual replacement. There was constant discharge about the anus and perineum, and intermittent passage of bright-red blood from the rectum. Severe constipation demanded the use of laxatives. This was followed by incontinence of feces and necessitated the constant wearing of an absorbent pad. Perineal discomfort, pelvic pain and backache were other complaints.

Rectal mucosa was visible at the anal outlet. The rectum descended 13 cm. through the anal orifice with straining, revealing a circularly grooved mucosa that was eroded and spotted with thick, white mucus. With cessation of straining the mass was reduced manually. The anal sphincter was atonic. Sigmoidoscopic examination was negative. General physical examination and laboratory studies were within normal limits.

Administration of sulfathalidine and crysticillin was begun on March 11, and 2 days later the Thiersch operation was performed. The postoperative course was marked by difficulty with defecation. Mineral oil and milk of magnesia were of no value. On the 3d day a warm-water enema gave unsatisfactory results. Castor oil by mouth followed by a cleansing enema was finally effective. A daily enema thereafter was adequate for bowel evacuation. The patient was discharged on March 22 and has had regular examinations since that time. At the end of 10 months there was no complaint and no evidence of recurrence. The patient is now able to perform all her daily activities satisfactorily and has become self-sufficient.

CASE 2. M. C., a 70-year-old woman, was admitted to the hospital on April 1, 1952, with the complaint of protrusion from the anus of 6 to 8 years' duration. She reported persistent whitish discharge about the anus, pressure in the pelvis and perineal discomfort. There was no rectal bleeding or pain with defecation. For many years she had noticed 3 or 4 loose stools in the morning. She was unable to carry on her work as a practical nurse because of the perineal protrusion and discomfort. Rectal treatments during the previous few years had been of no value in reducing the size of the protruding mass.

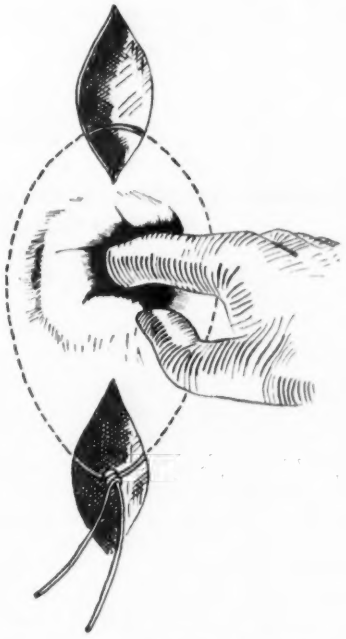

FIGURE 2. *Diagram after Needles Have Been Withdrawn. Wire is tightened about the index finger of the surgeon.*

Physical examination revealed a thin, well developed woman in no distress. The anal sphincter was markedly atonic, easily admitting several fingers. On straining there was descent of the rectum for a distance of 8 cm. through the anal orifice. This mass returned spontaneously on relaxation. System examination was otherwise within normal limits. Routine blood and urine studies were negative.

Sigmoidoscopic examination was negative. Barium-enema studies of the entire colon and terminal ileum were normal. On April 5 the Thiersch operation was performed, after preoperative preparation consisting of a low-residue diet, sulfasuxidine and streptomycin, daily enema and daily cleansing of the perineum with phisoderm. The postoperative

course was uneventful, and on the 5th day the patient was discharged from the hospital. Since operation she has taken a warm-water enema daily. Regular follow-up visits revealed no recurrence and no complaints at the end of 9 months.

CASE 3. A. W., a 68-year-old woman, was admitted to the hospital on August 19, 1952, with the complaint of rectal protrusion of 30 years' duration. In recent years the protruding mass had been present constantly, causing a pulling sensation in the lower abdomen, anal moisture and perineal discomfort. Occasionally, bright-red blood was passed by rectum. The bowels were irregular, occasionally constipated and frequently incontinent.

The patient was well developed and well nourished, reliable and co-operative. There was complete atonicity of the anal sphincter, with rectal mucosa visible at the anal orifice. On slight straining a mass bulged through the anus for a distance of 15 cm. This mass required manual reduction. System examination was within normal limits. Sigmoidoscopic examination was negative. Routine laboratory studies were normal.

Aureomycin had been prescribed for 2 days before admission, and this therapy was continued. A cleansing enema was given. On August 20 the Thiersch operation was performed. The patient was ambulatory at once and had an uneventful convalescence. She was discharged from the hospital on August 24. After 4 months the wire became slightly loosened; however, there was still no evidence of recurrence of the rectal procidentia. A warm-water enema every morning served to prevent the development of fecal impaction.

SUMMARY

The Thiersch operation is a simple palliative procedure advocated for the correction of rectal procidentia in the elderly, debilitated patient. Performed under local anesthesia the operation requires about fifteen minutes.

Three cases in which there were no complications or recurrences at ten months, nine months and four months after operation are presented. Despite the fact that the wire became loosened in 1 case there was no recurrence. These patients are happy and grateful and have been restored to a normal existence.

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MEDICAL PROGRESS

TUBERCULOSIS: INCIDENCE AMONG AMERICAN MEDICAL STUDENTS, PREVENTION AND CONTROL AND THE USE OF BCG*

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WITH the help of the Association of American Medical Colleges, a survey letter was prepared and sent to 71 four-year, Class "A" medical schools. This letter inquired into the incidence of tuberculosis among the medical students between 1940 and 1950, and the tuberculin testing, chest x-ray examinations and over-all prevention and control programs employed in those years. Data were received from 63 institutions — in unusable form from 1; no data were available from 1 school; they are still forthcoming from 2 others; and no answers were ever received from 5 institutions.

In addition, information on incidence, control and prevention was sifted from over 500 personal communications, and an attempt was made to determine the possible correlation between methods of prevention and incidence in these schools. Necessarily, the number of students and the periods covered by the reports vary; some schools included only a few hundred students in their records, and others surveyed 5000 or 6000. Finally, the medical literature of the last twenty years was reviewed with attention to the incidence of tuberculosis among medical students, the prevention and control of the disease in hospital personnel, the significance of acquired immunity and its reflection in tuberculin sensitivity tests, and the efficacy of BCG vaccination.

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REVIEW OF THE LITERATURE

Since 1931 many investigators have commented upon the "relative frequency" with which tuberculosis occurs among medical students. In 1931 Hetherington et al.[1] reported that medical students are peculiarly subject to tuberculous infection. Herman and his associates,[2] in 1932, remarked on the high incidence of tuberculosis at Western Reserve, Johns Hopkins and Pennsylvania medical schools. Madsen and his co-workers[3-8] have made many studies on the epidemiology, incidence and pathogenesis of tuberculosis, including in one report the contrast between the case rate among medical students (1.3 and 11.8 per cent) and that among other students of the same age group (0.4 and 2.6 per cent). Many other authors confirm these statistics, some of which are summarized in Table 1.

Dauer[9] concludes that the incidence of tuberculosis is greater among students of medicine than among persons in the same age group, and social and economic classes, and points out that the combination of most susceptible age group and heavy exposure rate is probably the chief cause of the increased incidence.

TABLE 1. *Incidence of Tuberculosis among Medical Students (Summary of Reports from the Literature since 1931).*

YEAR	AUTHOR	NO. OF STUDENTS STUDIED	INCIDENCE
			%
1935	Hetherington et al.[10]	400	4.2
1938	Malmros & Hedvall[11]	638	11.3
1938	Holm & Larsen[13]	1608	1.2
1940	Hart et al.[15]	349	6.1
1941	Alt et al.[16]	700	2.7
1941	Hahn et al.[18]	442	1.5
1941	Myers et al.[19]	305	5.9
1945	Daniels et al.[17] (Prophit Survey)	1547	1.7
1932	Steidl[10]	—	2.5
1940	Hetherington & Israel[10]	400	3.0
1940	Hetherington & Israel[10]	—	3.7–5.8
1939	Soper & Amberson[10]	1132	1.5–1.7
1939	Soper & Amberson[10]	427	2.5
1939	Soper & Amberson[10]	—	1.47–4.31
1941	Hahn et al.[21]	—	2.0
1943	Myers et al.[22]	1441	7.1
1946	Morris[23]	449	12.5
1947	Lees[24]	—*	—

*Medical students comprised 9 per cent of university enrollment and yet contracted 52 per cent of the cases of tuberculosis discovered in those years.

TUBERCULOSIS IN GENERAL POPULATION AMONG YOUNG ADULTS

In 1941 Plunkett and Katz[25] reported an incidence of 0.4 per cent among 7000 young women in New York state normal schools. The Metropolitan Life Insurance Company figures[26, 27] for 1940–1948, reveal that among 28,208 applicants for employment, there were 116 cases of clinically significant tuberculosis, or a case rate of 0.4 per cent. It seems that the case rate would be within 0.1 or 0.2 of this figure for the group between twenty and thirty years of age, since the great majority of job applicants were close to this age.[27] Robins[28] pointed out that there is usually no relation between mortality and morbidity figures, so that the mortality rates for medical personnel, which are low because of early diagnosis and thorough treatment, are not inconsistent with the high morbidity in the same groups.

The Prophit Survey,[17] presented in 1948, summarizes most of the valid surveys published up to that time on variation in incidence between medical students and other young adults. This survey also points out that Lees, at the University of Pennsylvania, described the incidence of tuberculosis among college students at 0.6 per cent as compared with 5.8 per cent in medical students. A few authors,[12, 21, 29-32] most of whom are also covered in the English survey, are not convinced of a significant, added risk for medical students. All in all, however, the authors of the Prophit Survey believed that most of this earlier work substantiated their own conclusion that the incidence of tuberculosis among medical students is significantly higher than that among other young adults. Their own work disclosed a rate three times greater among medical students than among comparable control groups.

RESULTS OF PRESENT STUDY

Our survey covered approximately 42,000 students from 62 medical schools; it involved 166,959 student years, all between 1940 and 1950, and uncovered 557 cases of clinical tuberculosis, a case rate of 3.34 per 1000 per annum. This constitutes a

TABLE 2. *Sixty-Two American Medical Schools, with Their Corresponding Number of Student Years and the Number of Cases of Clinical Tuberculosis Reported by Each School for Varying Portions of the Ten-Year Period between 1940 and 1950.**

MEDICAL SCHOOL CODE NO.	STUDENT YEARS	CASES OF CLINICAL TUBERCULOSIS
1	528	0
2	4426	8
3	5143	5
4	4785	57
5	4987	36
6	2270	1
7	1458	21
8	2755	20
9	969	3
10	3643	9
11	1831	4
12	1973	3
13	1428	4
14	2017	2
15	1094	0
16	4953	21
17	3079	3
18	3824	23
19	2403	3
20	1365	4
21	449	2
22	2521	37
23	4603	8
24	3169	1
25	2733	2
26	2605	2
27	3100	5
28	5521	61
29	1000	2
30†	4050	15
31	4054	2
32	929	1
33	1438	6
34†	2363	6
35	3300	2
36	3575	15
37†	3843	10
38†	2950	14
39	1644	1
40	3179	0
41	2947	9
42	5874	13
43	1002	4
44	4426	3
45	3225	2
46	5149	19
47	1113	4
48	2649	2
49	3043	6
50†	3489	20
51	2305	0
52†	2767	10
53	2443	2
54	3152	8
55	2349	2
56	985	0
57	892	1
58	734	1
59	1713	4
60	679	12
61†	2350	14
62†	1216	2
Totals	166,959	557

*Each school is identified by a code number since many have expressed this preference. It is only fair to state that all medical schools communicated with, except Arkansas, Southern California, Louisville, Syracuse and Temple, attempted to comply with our survey request.

†Incomplete or indefinite totals of cases.

variation from the incidence expected in a similar group not in medical school that is sufficiently beyond the standard deviation to be considered statistically "highly" significant.[33]

For comparative purposes some figures for the incidence of tuberculosis among the general population[17, 25-28, 34-53] were gathered and averaged. The group from twenty to twenty-nine years of age was selected since it includes most medical students. Predominant in the averaging were states with large urban communities and areas with known "high normal" tuberculosis incidence (including New York City and Massachusetts). Thus the average yearly case rate of 1.0 per 1000 young adults, twenty to twenty-nine years of age, is undoubtedly higher than a comprehensive figure including all the country's young adults in this age group. The standard deviation on these figures was calculated to be ± 0.4, so that the maximum yearly case rate conceivably to be expected in the group twenty to twenty-nine years of age would be 1.4 per 1000.

We have arbitrarily defined clinically active tuberculosis as that which is proved bacteriologically or that which evidences a lesion on x-ray study not apparent on earlier films and is accompanied by concomitant symptomatology, or both. All the patients included as having contracted tuberculosis fulfilled one or both of these criteria, and most required and received hospitalization for the disease. The schools that reported statistics on incidence for any part of the 1940–1950 period are given code numbers in Table 2. Next to each code number is the number of medical-student years for which the incidence of tuberculosis has been reported by the particular school. In other words, each (student-year) figure represents the sum of the numbers of students in attendance at one school during the years for which the incidence of tuberculosis was recorded by that medical school. Another column contains the number of cases of clinical tuberculosis discovered during the time reported upon.

The only manner in which the name of each medical school is recorded with its own corresponding tuberculosis incidence is in the original coded statistical tabulation that we compiled. This is done because there are many institutions that did not grant the authority to publish such data. The variations in yearly incidence among different schools were great, ranging from 0 to 15 per 1000. This was probably due in part to the differences in the method and accuracy of determining incidence at the various schools; the inherent failings of this method of investigation — although it was the only one that appeared feasible; and geographic factors. It is noted empirically that many of the schools reporting a low incidence of tuberculosis among their students recruit the great majority of their medical students from localized geographic areas that have a case rate in the general population far below the figures we have used for comparison.

Analysis of Data

We recognized the obvious difficulties and limitations inherent in this manner of study. The fact that the data from eight schools are incomplete provides an additional problem. However, it is thought that any possible error in this regard only tends to reduce the case-rate figures. In other words, a given incidence reported by a school in an indefinite or incomplete manner usually represents the number of cases of clinical tuberculosis that had been definitely recorded. The indefiniteness applies to cases not as carefully recorded. Also, in a number of schools a gap of three or four years occurs (usually coinciding with the war years) during which no records were kept or there was no case-finding program for tuberculosis among the medical students. Thus, it seems that if we err in this matter it is on the side of underestimation rather than exaggeration. The use of student years to determine the yearly case rate per 1000 removes many of the errors caused by differences in the time of student attendance and so forth that result from a simple percentage determination based on school admission figures.

The validity of these statistics we believe to be further enhanced by a number of facts. In the first place the general environment from which medical students emanate is a favorable one for producing young people resistant to the tubercle bacillus. This is true in terms of housing, food and physical condition, at least on entrance to medical school. (Physical well-being and considered ability to withstand four years of arduous study and training are criteria used in student selection by some medical schools.) Theoretically, at least, our figures should be compiled on a basis of time enrolled rather than student year. In other words, students who left school for scholastic or personal reasons were counted as though present for the same time as the rest of their class, whereas some of them obviously were not exposed to infection for as long a period; yet they are included among those who did not contract the disease. This also tends to incline our statistics toward an underestimation of the over-all incidence of tuberculosis in a medical-student population.

Tuberculin Sensitivity

The possible relation between tuberculin sensitivity and immunity to tuberculosis has been debated at length. For many years authors, here and abroad, have attempted to show the great susceptibility of negative tuberculin reactors to tuberculosis.[21, 30, 54-66] Some of the results pointing out the disparity in resistance between these two groups are summarized in Table 3.

Primary Infection and Clinical Cases

The observations presented in the Prophit Survey and by many different authors in different localities and reported under different conditions, in addition to the fundamental studies on immunity to tuberculosis reported by Rich,[70] Pinner,[71] Amberson[72] and others, leave one with the following inescapable conclusions: that there is great exposure to tuberculosis among students of medicine and nursing; and that liability to the development of clinical tuberculosis is much greater among those never before infected with the tubercle bacillus and now infected in medical training for the first time than among those who have been infected previously.

Primary infection in adults can be serious, and is often accompanied by symptoms of tuberculosis. Many cases of active disease follow shortly after primary infection. BCG vaccination should be the logical consequence, when progressive tuberculosis in adults seems to develop independently of a second exogenous infection provided that the vaccine confers the same protection as a primary infection and is itself relatively innocuous.

Table 3. *Resistance of Tuberculin Reactors to Tuberculosis.*

Author	Year	Incidence of Tuberculosis	
		positive reactors	negative reactors
		%	%
Madsen[64]	1942	1.3	11.8
Madsen[64]	1942	0.4	2.6
Heimbeck[65]	1938	3.2	13.8
Brahdy[66]	1941	0.5	3.7
Israel et al.[67]	1941	9.4	12.3
Wright[68]	1941	—	9.5
Meade[69]	1948	2.89	15.4
Dickie[55]	1950	4.3	13.6

BCG

The history of BCG, its definition, inception, development and improvement have been well described.[73-78] There are also good discussions of its theoretical and empirical value, and several reports of its use.[79-82]

Many personal communications have been received in the course of this study, all based on the experience of various physicians in dealing with tuberculosis among medical students and hospital personnel. Every report has emphasized the great incidence of disease among persons who convert from negative to positive reactors, the frequent cases of destructive or progressive pulmonary tuberculosis developing immediately from the so-called benign primary complex and the protection seemingly afforded by the use of BCG in addition to other preventive and control measures — a protection apparently lasting at least during the period of heavy exposure.

A study of the literature and these various personal communications have convinced us of the harmlessness of BCG and of the fact that it offers at least partial protection, particularly to the susceptible negative reactors subject to heavy tuberculous infection. It is undeniable that standard methods of prevention and control can be effective in greatly reducing incidence in hospitals. However, it is also believed that the elimination of all contact is not possible, for the following reasons:

Complete isolation is impractical today in most medical institutions, as well as harmful to the social and psychiatric rehabilitation of the patient.

Even when complete control and isolation have been attempted, there is still considerable tuberculous infection.

It is impossible to control future contact of medical personnel with the disease when they leave temporarily, or permanently, the strongly protected area.

Tuberculosis epidemics from a hidden source constitute a constant danger to the heretofore protected tuberculin-negative reactor.

It is possible for clinical tuberculosis to develop in a large proportion of those who convert from negative to positive reactors in spite of a greatly reduced infection rate so that reduction of infection rate, although important, is not the only objective.

BCG should not be offered as substitute prevention for control measures that have already been proved to be effective. BCG represents an additive weapon against tuberculosis, particularly as this disease threatens the nonimmune person when he encounters heavy tuberculous infection. Proper educational methods can prevent the use of BCG from creating a false sense of security. It must be impressed upon all recipients that the vaccine in no way constitutes complete protection and that all preventive measures to avoid contact and infection must be even more stringently employed in the future.

BCG also has its limitations. It is well realized that experience elsewhere (where living and health conditions are not optimal, perhaps) is not completely valid here. Also, more information is required about the basic structure and activity of BCG, and preparations that are standardized and more stable (less likely to allow mutation and so forth) are urgently needed. The tuberculin test is not yet properly uniform in dosage and interpretation of the antigens used; therefore, there is still variation in labeling an individual reactor or nonreactor. Because of this, it is sometimes difficult to know who can benefit from vaccination, and who can be vaccinated without excessive adverse reactions; more information on what constitutes a successful vaccination and how long the acquired sensitivity may last is needed.

All these mechanical limitations, as well as the arguments postulated by Myers et al.[22] and the fact that great advances have been made against tuberculosis in this country (largely without BCG), make it undesirable that BCG should be administered indiscriminately. This not only would reduce the now widespread diagnostic effectiveness of the tuberculin test, but also would make it difficult to plan controlled studies to determine scientifically the efficacy of the vaccine. However, the use of BCG on a limited scale, mostly in controlled studies and in susceptible groups highly exposed to tuberculosis, seems completely justified.

At the University of Michigan, Davey[83] has expressed the following view, with which we are in agreement:

> Because of the greater incidence of tuberculin conversion and the acquisition of active pulmonary tuberculosis by students of medicine and nursing in comparison with other individuals of the same age group, and because such individuals acquiring active pulmonary disease during the past ten years have done so at the time of their tuberculin conversion to positive in every instance (having thus been tuberculin negative reactors on entrance to the school), we, in the fall of 1949, instituted a program of BCG vaccination of the freshman students of nursing and medicine on a voluntary basis. Those students who were found to be tuberculin-negative reactors were offered the vaccination, and practically all have accepted.

BCG in Medical Schools

Table 4 summarizes the experience with BCG in the medical schools that employ it routinely as part of their tuberculosis-control program. It is interesting that of approximately 4400 students thus vaccinated, only 3 have contracted tuberculosis — none of whom became positive reactors. Not one truly vaccinated student out of 4400 with over 2 to 6 years of heavy exposure has contracted clinical tuberculosis. The occurrence of tuberculosis in only 3 students who had reverted to the non-reactor state or who had never converted to positive tuberculin reactors offers more evidence that some immunity is conferred by the hypersensitive state.

Table 4. *Use of BCG in American Medical Schools.*

Medical School	Period of Use yr.	No. of Students Inoculated	Adverse Reactions	Cases of Tuberculosis Occurring Among Those Inoculated
New York University	2½	38	0	0
Columbia University	4	175 (approximate)	0	0
Hahnemann Medical College	2	12	0	0
University of Pennsylvania	3	350	Occasional small persistent drainage (intracutaneous)	0
Woman's Medical College of Pennsylvania	4	133	0	1 case in girl whose reaction never became positive
Cornell University	2	10	5 small, nonpersistent drainages (intracutaneous)	0
Harvard	3½	227	Few low-grade drainages (last about 2 weeks)	1 solitary tuberculoma (present before vaccination)
University of Wisconsin	10	245 (plus 174 student nurses)	0	0
University of Illinois	8	228	0	0
University of Michigan	3	472	0	0
Tufts College	4	392	Few drainages (intradermal)	X-ray evidence of 2 pulmonary lesions of possibly tuberculous nature; both lesions static; students continued in school without treatment; both graduated in 4 yr.
University of Pittsburgh	3	254	0	0
University of California	5	78	0	0
University of Rochester	5	356 (plus 382 student nurses)	2 reactions: 1 ulcer lasting 2 mo., 1 keloid in student with tendency to keloid formation.	1 case in student reconverted to negative reactor; no revaccination; then lesion.
Washington University (St. Louis)	2	80	0	0
Western Reserve University	4	150	Slight drainage in 1 or 2 (no abscesses or lymph nodes)	1 case in student reconverted to negative reactor; no revaccination; then lesion.
Boston University	3	216	0	0
Duke University	3	90 (plus 60 student nurses)	0	0
University of Buffalo	6	200	0	0

Prevention and Control among Medical Students

Unfavorable Factors

Several factors have been implicated as probably contributing to the high incidence of tuberculosis among students of medicine and nursing:

Deficiencies in aseptic technic and sanitary methods because of ignorance or unconcern on the part of medical personnel themselves.

Inescapable, repeated contact with known tuberculous patients for purposes of education and patient care.

Contact with cadavers of tuberculous patients at autopsies.

Susceptibility of the age group involved and weakened natural resistance.

Unrealized contact with undiagnosed silent cases of tuberculosis.

We have attempted to prove that there is a higher incidence of the disease among medical students than should be expected. Part of the explanation for this fact is that the average tuberculin-negative medical student is in the age group in which the incidence of tuberculosis is high, lacks the immunity we have tried to show exists from previous infection and is heavily exposed to the disease for four to six years or more.

Suggested Remedies

The unfavorable factors can be overcome to some extent. Constitutional resistance can be greatly enhanced by improvement in the working and living conditions of the students and house-staff members. We have attempted to demonstrate that BCG vaccination affords added protection to this susceptible group.

Standard aseptic practices, in addition to a carefully managed program of health supervision of physicians in training, will help greatly to reduce the degree of exposure to the disease. Again, we point out the necessity of thorough education of the students involved. Medical students and house-staff officers not only must be aware of the importance of the standard aseptic procedures, but also must be impressed with the great need for their co-operation in a comprehensive, almost constant program of student health, tuberculin testing and x-ray examination.

Perhaps the most important factor in the incidence among hospital personnel is the undiagnosed case of tuberculosis. The only way to prevent contact with such sources is to discover these unsuspected cases earlier than seems possible in most general hospitals. It is suggested that the best means of offering this protection to medical personnel is to make routine chest films of every patient admitted to a hospital.

Medlar[84] has studied autopsies of 1235 persons dying suddenly. One out of every 20 of these had tuberculosis with cavitation; in only a fifth was it possible to find a prior record indicating that the person had had tuberculosis. On the basis of studies by Plunkett and Mikol[85] and Childress[86] one can estimate that 40,000 patients with unrecognized tuberculosis are admitted yearly to general hospitals in the United States. Oatway[87] reported that of 4539 general hospitals in the United States surveyed in 1948, only 247 reported that x-ray films were taken routinely of all patients admitted, the explanation usually given being the excessive cost of such a routine procedure. However, many observers point out that with the reduced cost of miniature x-ray film, there would probably be a budgetary saving over the cost of compensation paid to hospital personnel who contract clinical tuberculosis.

There have been many reports in recent years concerning the great reduction in costs of mass x-ray programs now that photofluorograms can be made for about 50 cents each. Also, in many places the local community organizations, tuberculosis societies and committees have been willing to buy the photofluorogram, and even to share the operating costs.[88] And yet, although it is impossible to overstress the importance of an x-ray examination in every admission, it should also be realized that all contact cannot be avoided unless medical students and nurses are not allowed to see patients before they are proved to be free of actual tuberculous disease. This is neither practical nor educationally beneficial to young people attempting to learn to recognize the disease. In addition to the patients' x-ray films, students of medicine and nursing must be educated to regard all patients as potential cases of tuberculosis, and their resistance to the disease must be afforded every possible assistance.

The institution of all the measures described above requires a well planned and thorough assault on the rate of tuberculous infection in hospitals and schools of medicine and nursing. This demands the hard work of many people and, in some locations, the added burden of extra x-ray expense. It is postulated, however, that the added work and energy are more than compensated for by the knowledge that all hospital employees, including young people preparing for a lifetime in the medical and nursing professions, are thereby less liable to the infection; and that the apparently additional expense is probably not a real one in view of the reduced costs of miniature x-ray films and the lower number of man hours lost, to say nothing of the costs of therapy and compensation.

The fact that such control programs prevent spread of this disease has been proved by Myers and many others. We wish to add the experiences of some American medical schools in recent years to the evidence that these preventive technics are more than worth their trouble in reducing the risk of tuberculosis to hospital personnel.

At the University of Illinois[89, 90] before World War II at least 2 or 3 medical students contracted clinical tuberculosis each year. In the last five years, a comprehensive control program (including the use of BCG) has reduced the incidence to 2 cases in five years. At Loyola University School of Medicine[91] there were 7 cases of tuberculosis between 1940 and 1943. In 1943 a student health service and a tuberculosis-prevention program were instituted, and there have been only 2 cases since 1943. The University of Kansas School of Medicine[92] has had no cases of tuberculosis among its students since 1940, at least partly because of a comprehensive control program. Tufts College Medical School,[93] utilizing a similarly excellent program (including BCG), has had no cases of tuberculosis in the last five years. At the University of Rochester School of Medicine,[94] a moderate incidence has been re-

duced to no cases since 1946 by the measures described above, including the use of BCG. Since the University of Texas[95] instituted a control program three years ago, only 1 case of tuberculosis has been discovered, whereas 5 to 7 cases a year had previously been found.

At Tulane University[96] the evidence is also dramatic: 20 cases of clinical tuberculosis between 1940 and 1946 and 1 case since then — an improvement owing to control intensification in the last four or five years. At Washington University of St. Louis[97] 9 cases of tuberculosis occurred among medical students between 1940 and 1947; since 1947, when a control program was intensified and BCG vaccination was added, there have been no cases of tuberculosis. At Wisconsin[98] prevention reduced the incidence of the disease, and BCG vaccinations have further lowered the case rate of clinical tuberculosis among medical students.

Reports from Woman's Medical College in Philadelphia[99] revealed a high incidence of tuberculosis before 1943 (18 cases between 1940 and 1942), and only 3 cases between 1943 and 1950. In 1943 a control program, which later included BCG, was instituted. At the University of Pennsylvania[100] there were 36 cases between 1940 and 1948. Since 1948, when prevention (including BCG vaccination) was emphasized, there have been no cases of tuberculosis. At Columbia University College of Physicians and Surgeons,[101] there were 6 cases between 1944 and 1948, when control was re-emphasized and BCG vaccination begun. There have been no cases of tuberculosis since then. University of Cincinnati College of Medicine[102] has had no cases since 1947, and Cornell[103] has had only 1 case since 1946 — both having instituted effective control programs. Finally, at the University of Minnesota,[104] where the results have been most gratifying, there has been only 1 case in the last seven years; before the institution of a thorough prevention system tuberculosis was discovered in 4 to 10 per cent of the medical students each year.

There seems to be no question regarding the effectiveness of these efforts. The institution of such measures at University of Rochester School of Medicine[94] not only accomplished the eradication of the disease from the medical-student population but also constituted in itself an excellent educational medium whereby the student is made acutely aware of the problem of tuberculosis and gains through personal experience definite training in the epidemiologic and public-health aspects of the control of tuberculosis.

Summary and Conclusions

The incidence of tuberculosis is much higher among medical students than among similar groups of young adults in the general population.

The primary complex is not necessarily benign. There is much evidence that it may directly precede progressive pulmonary tuberculosis or any complication, and therefore a re-evaluation of so-called minimal or benign disease seems necessary.

There is a much greater risk of clinical infection to the nonreactor on conversion to a positive tuberculin reaction than there is to the positive reactor. This indicates directly that some degree of immunity is conferred by tuberculin sensitivity and the previous infection that it represents.

Artificial sensitization by means of attenuated BCG vaccine is harmless and provides the same immunity as previous infection; protection is thus afforded the susceptible tuberculin-negative reactor, without the danger inherent in a focus of viable pathogenic tubercle bacilli.

The time-proved methods of control are reviewed. It is recommended that a routine program to prevent the disease among hospital personnel, especially medical students, student nurses and house-staff officers, be instituted in all hospitals. Chest x-ray examinations on all admissions are emphasized.

Because of the protection afforded, it is suggested that BCG vaccination be offered to all tuberculin-negative persons unduly exposed to the disease.

The part that each medical and nursing school can take, in offering tuberculin testing, chest x-ray films, contact avoidance, frequent checkups and BCG vaccination to its students, is described.

There is great need for the study of incidence and prevention to be carried to the house-staff level.

We are indebted to Drs. J. Burns Amberson, Allan M. Butler and Elliott Hurwitt for reading and editing of this material. Dr. Dean F. Smiley and the American Association of Medical Colleges were responsible for our being able to accumulate the data herein presented. There was generous co-operation and assistance from Drs. Elliott Hurwitt, Harry Zimmerman and Robert Bloch, of Montefiore Hospital, and from Drs. Leonard Goldwater, Alfred Gellhorn, Alfred Gilman and Harry Gruendfest and the late Dr. John S. Lockwood, all of Columbia–Presbyterian Medical Center. Grateful acknowledgment is made to the deans and health officers of the medical schools included in the survey. Above all, appreciation is due the members of the Association of Internes and Medical Students, whose enthusiasm and concern over this subject made the study possible, and to Mrs. Lee Abruzzi for her constant inspiration and untiring labor.

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MEDICAL INTELLIGENCE

KARTAGENER'S SYNDROME (SITUS INVERSUS, BRONCHIECTASIS AND CHRONIC SINUSITIS)*

Report of a Case

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THE triad of situs inversus, bronchiectasis and chronic sinusitis is known as Kartagener's syndrome. First reported by Kartagener in 1933,

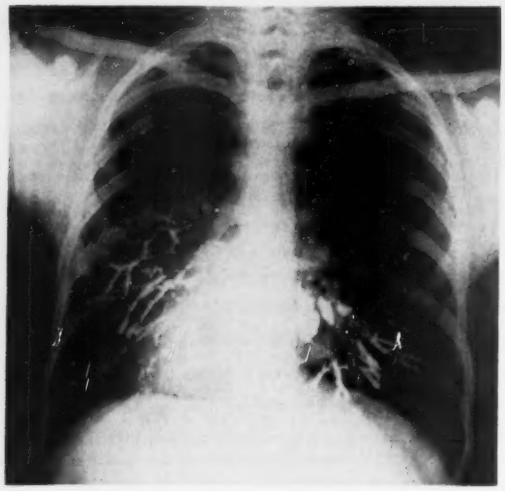

FIGURE 1. *Anteroposterior Roentgenogram of the Chest, Showing Dilated Bronchi Filled with Lipiodol.*

the syndrome had been described in approximately 40 cases up to 1951.[1]

The following case is presented as an additional example of the syndrome:

J. R., a 20-year-old Puerto Rican boy, was referred to the Kips Bay Chest Clinic by his physician because of frequent upper respiratory infections and a chronic, moderately productive cough. The cough had been present since childhood, particularly in the morning on arising. No hemoptysis had occurred. (He had had a chronic postnasal "drip" with frequent upper respiratory infections.)

A questionable history of pneumonia at the age of 13 was obtained. The patient denied that any members of his family had similar complaints.

Physical examination revealed a poorly developed boy. There was injection and edema of the nasal and pharyngeal mucosa with a postnasal "drip." Auscultation of the lungs disclosed subcrepitant rales and rhonchi at the right base and axilla. The apical impulse was palpated on the right side of the chest, and the heart sounds were heard on the right side. No cardiac murmurs or thrills were detected.

Fluoroscopy showed dextrocardia, with a patchy infiltration of the lung at the left base. Air in the fundus of the stomach was observed under the right leaf of the diaphragm,

FIGURE 2. *X-ray Film of the Skull, Showing Absence of the Frontal Sinuses.*

and a barium-swallow examination confirmed the impression of transposition of the stomach.

X-ray findings in the chest were similar to those noted on fluoroscopic study. Lipiodol instillation of the bronchi demonstrated a bilateral saccular bronchiectasis of the lower lobes of the lungs (Fig. 1). There was an absence of the frontal sinuses on an x-ray film of the accessory sinuses (Fig. 2).

Innumerable attempts to persuade other members of the patient's family to come to the clinic for examination were made without success.

The incidence of bronchiectasis occurring in persons with transposition of the viscera is significantly greater than that in the general population. Adams and Churchill[2] report 5 cases of bronchiectasis (21.7 per cent) in a survey of 23 patients with situs inversus totalis, with only a 0.03 per cent incidence in 250,000 general hospital admissions. Olsen[3] describes 14 cases (16.5 per cent) in 85 patients with dextrocardia observed at the Mayo Clinic during a twenty-seven-year period, 10 of the 14 having nasal polyposis. The increased incidence of bronchiectasis in situs inversus, a congenital anomaly, suggests a congenital factor in its pathogenesis. The occurrence of Kartagener's syndrome in twins and siblings would further support this theory. Whether a congenital predisposition or defect is an absolute prerequisite to the development of bronchiectasis is questionable, although it is apparently an important factor in some cases.

The lesions present in the nose and sinuses of patients with Kartagener's triad are varied. There may be mild or severe sinusitis, nasal polyposis

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and hypoplasia or agenesis of the sinuses. Kartagener and Ulrich,[4] in a study of a group of 86 patients with bronchiectasis, observed that the frontal sinuses were frequently very small or absent. The simultaneous occurrence of bronchiectasis and sinusitis was believed by these authors to indicate a co-ordinated constitutional factor in the sinuses and bronchial tree that is responsible for localization of infections there.

Cockayne[5] interprets situs inversus as depending on a single autosomal recessive gene. This is disputed by Torgersen,[6] who believes that transposition of the viscera is occasionally inherited as a dominant character, occasionally as a recessive one, and in many cases is not hereditary at all. He regards the predisposition to diseases of the nose and bronchi in patients with situs inversus as hereditary and probably caused by multiple genetic factors.

Kartagener's syndrome presents several practical considerations. Persons with situs inversus, especially with concomitant sinus infections, should be thoroughly investigated for bronchiectasis. The examination should include bronchography. The families of patients with Kartagener's syndrome should be screened for similar abnormalities.

Summary

A case of Kartagener's syndrome (situs inversus, bronchiectasis and chronic sinusitis) is described.

The factors and incidents relating to this syndrome are presented.

Some practical suggestions are given for discovering more cases through bronchography, x-ray films of the sinuses and survey of the families of patients.

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PRACTICAL USE OF COLOR IN CLINICAL DIAGNOSIS*

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COLOR differentiation is in constant use in determining results of various tests in the modern clinical laboratory. It appears worth while to mention the practical value of color perception in an earlier stage of diagnosis — that is, history taking — and to suggest a simple means, handy for daily use by the physician, of obtaining important information.

Major points can frequently be gained by utilization of the patient's appreciation of color. Excretions from the body orifices and medicines and household substances taken orally are the main categories in which one may need to establish a definite color relation. Rarely, individual development of pigmentation in the skin, gums or scleras may be of value in the past or family history. Many patients give vague descriptions of color and are happy to be confronted with a selection from which they may choose. The use of a chart with various colors in several shades helps the physician decide whether

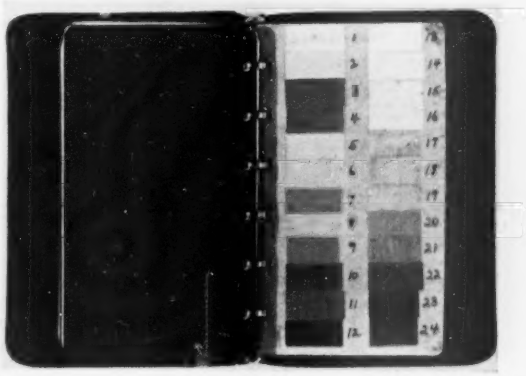

Figure 1.

"dark specks" in sputum may have been old blood or carbon particles, whether "red" urine was due to excessive hemolysis or to hemorrhage, whether a "light stool" was more probably the yellowish appearance associated with pancreatic disease or the gray usually seen in biliary-tract obstruction or infectious hepatitis, whether a "green tablet" was the grayish green of digitalis or the bright blue green of pyribenzamine and so forth.

In addition, there are patients whose history is sketchy because of educational or intellectual inadequacy or a serious language barrier. The last of these is encountered more frequently in the larger cities; it is certainly not uncommon at the Pennsylvania Hospital and is quite frequently mentioned in the Case Records of the Massachusetts General Hospital in this journal. In such cases the examining physician can often gain essential information by using elementary sign language and displaying a chart for the patient to select the proper color.

Most doctors carry a reasonably substantial notebook or prescription pad, and it is an easy task to make a color chart to fit. In only a few minutes a wide range of color samples can be collected from the advertisements of one or two outdated magazines. Ten different shades varying from pale yellow to

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dark brown, six shades of red from pink to deep maroon, three shades of green, two shades of blue, two shades of gray and one pitch black are sufficient. The aid of wives, children, secretaries or patients may be solicited to complete the job of trimming, arranging and mounting in the desired color groups. A fairly sturdy page is advisable as a base for the mounted samples owing to the traumatic effects of use. A piece of cardboard is quite adequate for looseleaf notebooks. Covering the entire chart with cellophane provides added protection and prevents soiling. A color chart of this nature, 3 by 5 inches, has served well for the past two years (Fig. 1).

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 39171

PRESENTATION OF CASE

A fifty-six-year-old single woman was admitted to the hospital because of anorexia and weakness.

Two months before admission the patient became aware of weakness, easy fatigability, anorexia and afternoon fever. She had also experienced occasional night sweats, and a nonproductive cough had developed. She was treated with liver and iron, but because of diarrhea the medications were stopped; thereafter the diarrhea ceased. Her general status did not improve, however, and she was admitted to another hospital, where a roentgenogram of the chest showed a left pleural effusion. A thoracentesis was performed, but no fluid was obtained. She had lost 25 pounds in weight during the present illness.

Eight years before admission the patient had a severe cold accompanied by fever, cough productive of yellow sputum and dull pain over the entire chest, which lasted four weeks and then cleared completely. Five years before entry soreness over the back developed in the region of the left-lung base. The spot was tender, and unaffected by respiration. A chest film showed fluid in the left base, which was seen to have cleared in a second roentgenogram. There was no history of dyspnea or hemoptysis and only slight soreness over the left-lung base posteriorly. There was no melena, diarrhea, change in bowel habits or sweating.

Physical examination revealed a thin, pale woman who appeared chronically but not acutely ill. The skin was warm and not icteric. There was no lymphadenopathy. The left-lung base showed slight dullness and diminished breath sounds. There were no rales or egophony. The heart was of normal size; the aortic second sound was greater than the pulmonic, and there was a Grade 1 basal systolic murmur. The abdomen was distended, but there were no palpable organs or masses. There was no free fluid. Pelvic and rectal examinations were negative. There was no cyanosis, clubbing or edema of the extremities.

The temperature was 100°F., the pulse 120, and the respirations 24. The blood pressure was 90 systolic, 56 diastolic.

The urine had a specific gravity of 1.020 and was normal. The urine urobilinogen was 0.5 units. Examination of the blood showed a hemoglobin of 8.2 gm. per 100 cc. and a white-cell count of 17,200, with 86 per cent mature and 3 per cent immature neutrophils and 11 per cent lymphocytes. The chemical determinations were normal except for a carbon dioxide of 29 milliequiv., sodium of 127 milliequiv. and potassium of 4.1 milliequiv. per liter. The prothrombin time was 14 seconds (normal, 13 seconds). Of six stool specimens all were brown but two gave ++ and four gave ++++ guaiac tests. Old tuberculin tests (1:100,000 and 1:1000) were negative.

An intravenous pyelogram showed the kidneys to be normal in size, shape and position. The contrast substance was excreted promptly and in good concentration, outlining nondilated upper urinary passages. The bladder was not unusual. An irregular density thought possibly to be a uterine fibroid or feces in the sigmoid was present in the left side of the pelvis. There was a rounded, rather poorly outlined mass measuring approximately 12 cm. in diameter lying in the right side of the abdomen just above the iliac crest. The central portion was less dense than the periphery and appeared to contain a linear calcification about 1.5 cm. long. The mass appeared to displace the ascending colon laterally and possibly the right ureter slightly medially. The right-psoas-muscle shadow and both properitoneal fat lines were distinct. Plain films of the abdomen showed a fluid level measuring 7 cm. wide in the center of the previously described mass in the right lower quadrant (Fig. 1). Several smaller fluid levels were present in slightly dilated loops of small bowel in the left side of the abdomen. On barium-enema examination the barium passed

readily from the rectum to the cecum and refluxed into the terminal ileum. No obstruction was encountered, and the postevacuation film revealed that the mucosal pattern was normal throughout. The ascending colon and right portion of the transverse colon appeared to be displaced laterally by the mass in the right side of the abdomen (Fig. 2). In the pre-evacuation film, the cecum and terminal ileum appeared to be compressed by the mass. The bones and soft tissues were not remarkable. In a gastrointestinal series Urokon was passed through a Harris tube into the stomach (Fig. 3). The stomach and duodenum were normal. The contrast substance passed completely through the small intestine and was probably present in the cecum at the end of three and a half hours. No markedly dilated loops of bowel were seen. There was a poorly defined area in the right lower quadrant measuring 8 cm. in greatest dimension that appeared to be a cavity containing fluid and air; this cavity filled with Urokon within thirty minutes of the start of the examination, emptied, refilled within the next hour and emptied again within the next hour.

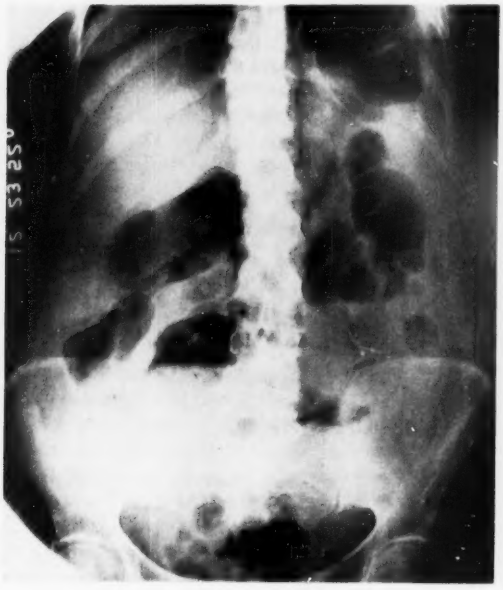

FIGURE 1.

On the sixteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD SCHATZKI*: I shall start with the disease that was the oldest in this patient's history — the lung condition. In the chest films taken on admission the evidence of disease is meager. The left leaf of the diaphragm is slightly elevated, and there is some process in the lung close to the diaphragm that is seen on the film taken in the anteroposterior position. Since the left leaf of the diaphragm is not visible anteriorly, there is apparently some disease fairly far anteriorly on the left side. I cannot see any fluid, and I doubt if fluid was present on the previous occasions. I do not know what this is; it could be an infarct. The patient may have had multiple infarcts in the past. This could be a small area of atelectasis of undetermined cause. In any event, in spite of the emphasis that the history puts on the chest condition, I cannot see that it bears on the major problem of this patient's illness. The only possible connection that I can make between this chest condition and the later disease in the abdomen is to say that this could have been actinomycosis and that the patient had actinomycotic abscesses in the abdomen. This does not look like actinomycosis, and the process did not act like actinomycosis, so I shall forget about that and assume that the chest disease was not connected with the illness. I hope I have not burned my bridges too early in the game.

FIGURE 2.

In the plain film of this patient's abdomen (Fig. 1) there is an air-filled cavity on the right side; it is approximately round, has a scalloped, irregular

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edge and contains a small area of calcification. No definite mass is seen outside this air-filled cavity. There is another air-filled and fluid-filled cavity on the left side. A film in the upright position demonstrates, in addition to the fluid level in the right cavity and the small fluid levels in the bowel mentioned, an indistinct, fluid level in the cavity on the left side. The barium-enema examination (Fig. 2) shows displacement of the ascending and transverse colon by the process in the right side of the abdomen and, I think, slight displacement of the sigmoid by the disease in the left lower

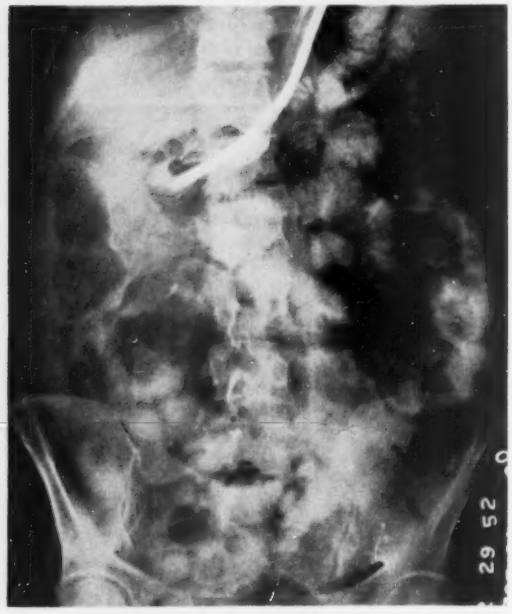

FIGURE 3.

quadrant. This small fecalith or density in the left pelvis that was described is not visible on all the films, and I am going to abandon the idea that it may have been significant. In the intravenous pyelogram, as the record says, there may be some displacement of the right ureter toward the midline, but that is not too definite. The marked scalloping of the inside of this cavity is clearly visible. The films selected from the series in which Urokon was passed by mouth through the Harris tube (Fig. 3) demonstrate the cavity on the right to be still filled with air and the one on the left side to be filled with dye. Later, the cavity on the left side empties, and the one on the right shows a small amount of dye along the edges of the cavity.

In other words this patient had two abnormal cavities in the lower abdomen — at least I think they were cavities. Except for cavities there is only one lesion in the abdomen that could conceivably have produced a picture with a density like this and that would have been likely to have calcification in it; that is a dermoid cyst or teratoma of the ovary. Such lesions contain sebaceous material, which is fluid at body temperature and can form a fluid level when the films are taken in an upright position. I think I can exclude dermoid cyst for all practical purposes because the density in the x-ray film is more brilliant than that of fat — it has the brilliancy of air or gas. Furthermore, there is only an outside chance that a dermoid ulcerated into the bowel and produced this appearance.

One word about the calcification: it looks unusual and should have some significance. I can think of many possibilities but none as definite as the dermoid that I have ruled out. Possibly, a foreign body could perforate the wall of the bowel, become calcified and lie in this cavity. I think that is very unlikely.

A few additional x-ray studies might have been helpful. One could have taken films with the patient lying alternatingly on the right and the left side to see if the two cavities were connected — that is, if by gravity the air went from one to the other. One could have taken films with the head hanging almost down to study with the help of air the bottom of the cavity or of whatever this process was. Finally, I wonder if there was enough evidence of obstruction to warrant refraining from using barium by mouth in this particular case. I doubt if there was, from the plain film. Obviously, more information would have been obtained from the use of a substance of the density of barium than from a substance of the density of Urokon. At fluoroscopy, if a tube had been inserted in the duodenum and a small-bowel enema had been given, the relation of the bowel to the two cavities might have been apparent.

What type of cavities do I have to think about? Could these have been diverticula? Diverticula of the small bowel are not rare, and may be extremely large, particularly Meckel's diverticulum, which may have tremendous dimensions. Against Meckel's diverticulum is the position, which would be unusually high. Moreover, the inside of these cavities was too irregular for me to assume that they were diverticula unless one assumes secondary tumor formation in diverticula, but that is so rare that I think I can forget about it. The same statement applies to congenital anomalies such as reduplication of the small bowel.

The two possibilities that I have to discuss are abscess cavities and tumors that become ulcerated and connected with the bowel lumen. In favor of abscess are the clinical features; the patient obviously had infection with fever, and a high white-cell count; also in favor of abscess is the absence of a palpable mass, which is quite disturbing. The

fluctuant character of material of the cavity could very well be explained by the presence of pus in this cavity. Finally, I think of the rare abscesses like tuberculous abscess from a large tuberculous lymph node that had perforated into the bowel. I think that is practically though not completely excluded by the negative tuberculin tests; it would be very unusual anyway. I have more or less discarded actinomycosis. What speaks against abscess? The anemia was quite severe for so little infection. The patient was obviously bleeding into the bowel, which would be unusual for an abscess. Furthermore, a real cause for an abscess is missing. There was no acute story of ulcer or gallbladder disease that might have caused an abscess in the abdomen; it is possible that there was a low-grade smoldering abscess from an appendix. The point especially against abscess, however, is the fact that in spite of the communication of the cavity with the small-bowel lumen, the patient was still sick. I should imagine that the patient would have cured herself if an abscess had been connected with the small bowel. Although abscess is still a possibility, some features are difficult to explain by it.

If this was tumor, there are two main possibilities to consider: tumor of the small bowel and tumor outside the small bowel, which had become connected with it. Of the tumors of the small bowel cancer is somewhat unlikely. Too much of the disease seems to have been outside the lumen for cancer. It is possible that a huge cancer ulcerated outside the bowel, but it seems less likely than an intramural extramucosal tumor like leiomyoma, fibroma or leiomyosarcoma, which had become ulcerated and more or less completely emptied into the small bowel. That would adequately explain the anemia. The first symptom in these tumors is usually anemia. There are a few difficulties; one is the infection that this patient had, and we would have to assume that there was superimposed infection present; and the other is the absence of a palpable tumor mass. The only explanation for that is that because the patient was distended by the ileus, it was difficult to palpate the tumor, which was probably soft and necrotic.

Among the tumors outside the bowel that may become connected with the bowel is ovarian cancer, which sometimes ulcerates into the bowel and may empty into it. I have seen such a case. I cannot imagine that a degenerated fibroid of the uterus would do that; it would be quite unusual.

Finally, I can imagine that a lymphoma of the bowel cavity grew into the bowel wall, became attached to the wall and acted like any small-bowel tumor, which is likely to become necrotic from the digestive power of the inside of the bowel at this particular level. A slight ischemia is sufficient to start this ulceration; once it is started it may increase like wildfire in a poorly vascularized tumor.

As I summarize the possibilities, I believe the chest lesion had no connection with the abdominal disease. I shall put first a tumor that had become ulcerated and emptied into the bowel. Whether this was an intrinsic tumor of the bowel or a tumor that had secondarily involved the bowel, I do not know. I shall place an intramural extramucosal tumor as my first choice. Primary abscess is a possibility but considerably less likely.

Dr. Edward B. Benedict: How about a mesenteric cyst or a peritoneal cyst?

Dr. Schatzki: I should have mentioned that. It belongs in the same group as duplication of the bowel as far as the mechanism is concerned. Against such a diagnosis is the fact that the lumen of the lesion was connected with the bowel lumen and furthermore that the inner surface of the lesion was irregular.

A Physician: How did you explain the high white-cell count?

Dr. Schatzki: It is difficult to explain, but I assume that secondary infection was present.

A Physician: What would an echinococcus cyst look like?

Dr. Schatzki: That thought went through my head, too, as I thought about this case. I forgot to mention it. An echinococcus cyst could become connected with the bowel and could look very much like this. It is considerably more irregular on the inside than all the other cysts and could possibly produce all these symptoms. However, echinococcus cyst would be extremely rare in a native-born American who never left this country.

A Physician: Does the negative tuberculin test rule out tuberculosis?

Dr. Schatzki: The phthisiologists tell me that unless the patient is very sick it is a reliable test. In my own experience it is not quite that reliable, but I think there are other features that make tuberculosis unlikely.

Clinical Diagnosis

?Carcinoma of lung.
?Carcinoma of intestinal tract.

Dr. Richard Schatzki's Diagnosis

Intramural extramucosal tumor of small bowel.

Anatomical Diagnosis

Leiomyosarcoma of jejunum with cystic degeneration.

Pathological Discussion

Dr. Benjamin Castleman: At the operation a large mass was found adherent to a loop of jejunum, a loop of ileum and a piece of the transverse colon. The mass was huge, measuring 15 by 14 by 6 cm., and on sectioning was cystic. When the bowel was opened there was a large perforation about 2 cm. in length, the margins of which were covered with fibrin that extended into the large tumor. The

tumor had produced necrosis of the mucosa, and there was a direct perforation that led into the large cystic cavity, which had a shaggy fibrinous lining indicating severe infection. Apparently, there were two cavities connected with each other owing to cystic degeneration or cystification of the tumor. As Dr. Schatzki predicted, this was an intramural extramucosal tumor, a quite rapidly growing leiomyosarcoma, with numerous mitoses. As far as I can tell from the operative note — I was unable to talk with the surgeon — the tumor was entirely removed en bloc with the various sections of the bowel attached. Although it was attached to the ileum and transverse colon, there was no extension into the walls of either, so there is no question that this arose from the wall of the jejunum.

DR. ALFRED KRANES: Was there one mass or two?

DR. CASTLEMAN: One. It is surprising that the mass was not felt.

DR. SCHATZKI: How did the mass feel at operation? Did the surgeon make any mention of that?

DR. CASTLEMAN: Dr. Canada, did you see the operation?

DR. WILMA J. CANADA: I think the surgeon said it felt quite soft. It was difficult to identify.

DR. CASTLEMAN: It was on both sides of the abdomen?

DR. CANADA: Yes.

DR. SCHATZKI: How much of the tumor mass was actually cavity, and how much was solid?

DR. CASTLEMAN: Most of it was solid tumor.

CASE 39172

PRESENTATION OF CASE

An eighty-one-year-old man was admitted to the hospital because of pain across the chest.

The patient had been in excellent health until two weeks before admission, when he first experienced pain in the left posterior scapular region. Later in the day he felt pain in the right posterior scapular region as well as down the spine. During the next four or five days he also had pain across the shoulders and pectoral region. The pain was a sharp, severe, steady ache, which on occasion awakened him from sleep, became more severe when he coughed and frequently appeared if he moved suddenly, although it was not definitely related to position. Usually, it lasted one to two hours, disappeared, and then returned in six to eight hours. During the week before entry attacks had become increasingly more frequent. Three days before admission he experienced pain down the entire right leg, front and back, and two days later pain in the left leg. On further questioning the patient about his legs, the examiner could not be certain that the patient was not confusing pain with weakness. About ten days before entry the patient's gait became unsteady, and he became progressively weaker. Five days before admission he was barely able to walk a short distance around the house. On the next day his knees "buckled," and he fell. He began to use a cane because of unsteadiness, but on the morning of admission his legs "buckled" again and he was unable to walk without support. Three days before admission he had complained that his right lower leg felt cold and numb over the anterior aspect.

The patient was able to use his arms and had no weakness or paresthesias of the upper extremities. Two years before admission he had fallen from a second floor, landing on the base of his spine; he had no immediate symptoms. Three years before entry he had an abdominal hernia repaired. At that time the blood pressure was 125 systolic, 80 diastolic, and routine laboratory studies were normal. The past history and systemic review were otherwise noncontributory.

Physical examination disclosed a well developed and wiry man. During the examination he had a severe pain across the upper anterior portion of the chest lasting five minutes. There were bilateral cataracts. On movement of the neck there was slight restriction laterally, but this did not cause pain. The lungs were normal. The heart was not enlarged, and the aortic second sound equaled the pulmonic. The heart sounds were faint but seemed normal. The abdomen was normal. There was a firm nodule in the middle lobe of the prostate 4 mm. in diameter. This was unchanged since the admission three years previously. Positive neurologic findings included moderate weakness of the left leg and a lesser degree of weakness of the right leg. Muscle tone was normal. Tendon reflexes were weakly present in the arms but absent in the legs; there were bilateral extensor plantar reflexes. There was diminished pain sensation in the right leg from the fourth or fifth lumbar to the second sacral dermatome. Position sense was diminished in the toes of the right foot.

The temperature and pulse were normal; the respirations were 25. The blood pressure was 220 systolic, 122 diastolic.

The urine was normal. Examination of the blood showed a hemoglobin of 16.3 gm. and a white-cell count of 11,800, with 90 per cent neutrophils, 7 per cent lymphocytes, 1 per cent monocytes, and 2 per cent eosinophils. The serum calcium was 9.6 mg., the phosphorus 1.1 mg., the alkaline phosphatase 3.7 units and the acid phosphatase 1.8 units per 100 cc. A roentgenogram of the lower cervical and upper dorsal spine demonstrated marked osteoarthritis involving the middle cervical and upper dorsal spine, with narrowing of the contiguous intervertebral disks between the lower four cervical vertebras. There was no cervical rib. A roentgenogram of the chest revealed extensive pleural calcification in the right thorax, chiefly anteriorly and

in the upper half. The lungs appeared normal. Films of the thoracolumbar spine and pelvis showed only fairly extensive hypertrophic changes. A lateral view of the skull was normal.

On lumbar puncture at myelography, clear, colorless spinal fluid containing 171 red cells and 2 white cells per cubic millimeter was recovered. The total protein was 248 mg. per 100 cc. The constant substance did not pass beyond the junction of the twelfth thoracic and first lumbar vertebras (Fig. 1).

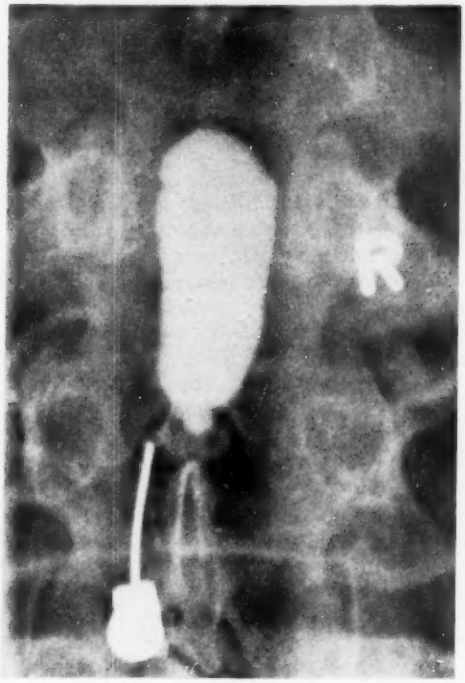

FIGURE 1. *Lumbar Myelogram before Laminectomy, Showing Complete Block at the Twelfth Interspace.*

On the second hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. JAMES B. AYER*: May I look at the x-ray films now?

DR. JOSEPH HANELIN: The original films of the cervical and thoracic spine, made in another hospital, show extensive osteoarthritic changes. There is a localized scoliosis to the left in the upper thoracic region and some lateral wedging of the third thoracic body and perhaps also to a slight degree of the fourth. Any evidence of actual destruction is at best equivocal. There is perhaps slight alteration of the pedicles of the third thoracic vertebra, which are not as clearly defined as those above and below, but there is no widening of the interpediculate distance.

DR. AYER: The sharp scoliosis is at the second thoracic vertebra.

DR. HANELIN: The cervical spine shows severe degenerative changes, with narrowing of the disk spaces and considerable spur formation. The chest film, made with the patient in bed, demonstrates extensive calcification of the pleura, which is unchanged compared with an examination done in this hospital three years before admission, and the lungs are otherwise clear. The lower thoracic spine shows little osteoarthritic change. There are large spurs in the lumbar region. The skeleton is fairly well calcified, particularly for a person of this age. The pyelograms demonstrate a complete block at the twelfth thoracic interspace (Fig. 1); the edge of the column is nondescript. I think it would fit a subarachnoid type of block rather than an extradural one.

DR. AYER: There is no Pantopaque beyond?

DR. HANELIN: Not beyond that level.

DR. AYER: Did it all go back?

DR. LOUIS L. BAKAY: It went back perfectly normally.

DR. AYER: In this case the initial pain in the upper part of the chest and back was bilateral in character; the attacks increased in frequency and severity during a period of two weeks and were followed after eleven days by pain in both legs accompanied by rapidly progressive weakness of both legs. Before the eleventh day there was some weakness of the legs. The whole episode of pain went on for two weeks before operation.

I am dealing with symptoms in the upper dorsal region and symptoms in the lumbar region, foci that, if caused by lesions in the spinal cord, represent foci quite a way apart. Were these symptoms in the chest and in the lumbar region due to the same or to different conditions? In the history and the x-ray examination I find no good cause outside the spinal cord or nerve roots for pain in the dorsal region. The Babinski reflex could have been due to a lesion in that region and should not have been due to what was found in the lumbar region. There was no evidence, either by x-ray examination or from the symptoms, of marked heart or lung disease, aneurysm or anything else in the chest that was likely to have caused the severe pain through the chest. It certainly does not sound like angina. The attacks were increasing in frequency and severity, and there are a good many points that suggest root pain. I shall not go into that because it would take us fairly far afield. Nerve-root pain is frequently bilateral. I therefore believe that I am on safe ground in assuming that the pain in the chest and upper back that started

*Member, Board of Consultation (formerly, chief of Neurology Service), Massachusetts General Hospital.

this all off was probably from the same cause as the leg symptoms and implies a rapid extension of the pathologic process.

In the legs, there was objective evidence of involvement of the low spinal cord or the nerve roots of the cauda equina or both, as shown by the rapidly developing weakness, absence of reflexes and, finally, weakness to the point where the patient had to use a crutch. The urinary bladder was not mentioned; certainly it should have been affected. The myelogram shows a block in the region of the twelfth thoracic and first lumbar vertebras. I am in agreement that the x-ray films are not suggestive of a subdural tumor, which would probably have pushed the spinal cord to one side; they are more in favor of a lesion outside the dura. That is a point I did not know until I saw the films. How much higher this block extended, I do not know. Pantopaque by cisternal puncture would have revealed this important point. That the disease did extend higher is indicated by the bilateral Babinski signs.

If the argument up to now is sound, I am dealing with a pathologic process of considerable extent compressing the spinal cord and nerve roots, or with two foci of disease, one upper dorsal and the other lumbar in location. There is no indication about the exact nature of the disease process. The one thing that was mentioned is against a diagnosis that I certainly favor. The patient's prostate was large but was the same size as it was two years before admission, and the acid phosphatase was within normal limits — both are evidence against prostatic cancer.

There is so little evidence that I have to make a diagnosis more or less by elimination and on the basis of previous experience. I am going to run briefly through the various lesions we have seen and present evidence for disregarding them.

There are three diseases of the spine that have the habit of breaking through the spine into the epidural space and causing spinal-cord compression. One is osteomyelitis, which should be of long standing. Since there is no evidence for that, I shall rule it out. Cancer of the spine itself may erode and cause epidural deposits. There was no evidence of long-standing cancer. Tuberculosis is the commonest disease of the spine that erodes into the epidural space. There was no evidence of Pott's disease. It seems, therefore, that a vertebral origin for this spinal-cord compression is most unlikely. Although I cannot rule out diseases of the spinal column, the process here occurred too rapidly to be characteristic.

The second condition is disease infiltration through the intervertebral spaces, without invasion of the bone itself. This is not uncommon in epidural abscess arising somewhere else; for instance, a dermatome infection of the skin will sometimes follow the nerve roots or lymphatics into the epidural space without visible changes in the x-ray examination. Against that was the lack of fever, the white-cell count of 11,000 and the absence of cells in the spinal fluid. With infection, there should be a boggy, quite tender back; this was not mentioned. Different types of granulomatous tissue may also be found in the epidural space extending up and down the spinal cord. Granulomas, however, usually do not develop as rapidly as this. Lymphoma is another form of tumor that may show nothing on x-ray examination. With this history of a fall two years before admission one might consider a diagnosis of ruptured disk. Ruptured disks compress the cord or cauda equina in rare cases. In fact Goldthwait,* in 1911, described such a patient. It would imply a large ruptured disk, which would cause the pain to come on this suddenly. Such disks have been operated on with a preoperative diagnosis of tumor. A disk might be present in the lumbar region, but two disks compressing the cord at different levels and both producing bilateral lesions would be unlikely.

Benign tumors should be considered. One condition that would cause symptoms up and down the cord is multiple neurofibromas. I have never seen them produce symptoms so rapidly as this, nor do they usually compress the cord. The same statement is true of arachnoid fibromas arising from the arachnoid.

Inside the epidural space, in the meninges, there may be one of two conditions, neither of which seems to have been present here. The first is block with symptoms up and down the cord from an old infectious meningitis, but there was no history or signs of meningitis. Another is hemorrhage, a diagnosis that I missed two years ago at a Clinicopathological Conference. Hemorrhage may run up and down in the subarachnoid space, causing compression of the cord and of the roots and pain very much like this patient's. No blood was noted in the spinal fluid, and it seems most unlikely that the blood would have been held above the block; the spinal fluid was not xanthochromic. Hemorrhage, of course, should have occurred much more suddenly; this was rapid, but not sudden. I should think hemorrhage was ruled out. Also, a malignant glioma may run up and down the meninges, causing some of these symptoms, but not quite so rapidly and not causing compression until very late. We had such a case here some time ago.

Lesions within the spinal cord such as syringomyelia and intramedullary tumor produce this picture, but those processes are much slower, and on this alone I shall rule them out.

The evidence at hand points to a rapidly extending pathologic process in the epidural space such as lymphoma, and I say this because it is the commonest one; secondly, granuloma, which is rare; and thirdly, two or more foci of metastases from

*Goldthwait, J. E. Lumbo-sacral articulation: explanation of many cases of "lumbago," "sciatica" and paraplegia. *Boston M. & S. J.* **164**: 365-372, 1911.

cancer. Although the evidence for prostatic carcinoma is extremely poor, — in fact one could almost say it was not prostatic carcinoma for the reasons given, — it is the commonest tumor that spreads directly into that particular area of the lumbar region, but there would have to have been a blood-borne metastasis to the cervical region, which rather bothers me, or an extension upward with symptoms occurring early in the cervical region, which is unlikely.

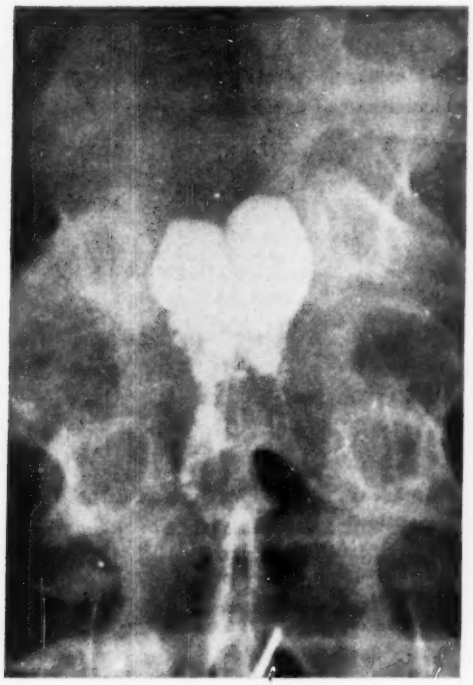

FIGURE 2. *Lumbar Myelogram after Lower Thoracic Laminectomy, Showing Persistence of Pantopaque Block Despite the Negative Exploration.*

DR. EDGAR B. TAFT: As Dr. Ayer suspected, this patient had a laminectomy on the second hospital day over the eleventh and twelfth thoracic and first lumbar vertebras, and nothing was found. I think everyone was rather surprised. The surgeon who treated him was able to push a catheter downward about 17 cm. and upward about 21 cm. within the dural space without meeting obstruction, although there seemed to be some obstruction in the neighborhood of the third thoracic vertebra. He thought that the twelfth thoracic vertebra was angulated forward on the first lumbar vertebra and that the myelogram might be explained on that basis. He could not see any actual anatomic obstruction. The patient did fairly well postoperatively and a repeat myelogram demonstrated the same complete block at the twelfth thoracic vertebra (Fig. 2).

DR. HANELIN: A second myelogram done through a cisternal puncture demonstrated a complete block at the second and third vertebras.

DR. TAFT: The surgeon then did a second laminectomy. At the time of operation the pathologist thought he found tumor cells on frozen section, but when the fixed sections came through there was no tumor in the tissue that was removed from around the dura. Jaundice developed, probably as a result of multiple transfusions. On the sixteenth day Dr. James C. White thought he could demonstrate a sensory level at the fifth thoracic segment on the right and at the twelfth thoracic segment on the left, but there were no further remarks in the record about this. On the twentieth hospital day the patient was found pulseless, pallid and unresponsive and without respirations. He was given artificial respiration and oxygen. He started breathing again and complained of pain in the right leg, but he again became unresponsive and died forty-five minutes later.

The clinical impression was that he had an extradural malignant tumor, probably metastatic, which might have come from the prostate, and that he died of a pulmonary embolism.

DR. RAYMOND D. ADAMS: In the second operation Dr. White observed that the spinal cord was displaced posteriorly by a mass lying anterior to it; he tried to approach this mass from the side but did not succeed in moving the cord. He was sure the mass was an epidural tumor. No tumor was found in tissue removed for biopsy.

CLINICAL DIAGNOSES

Extradural malignant tumor,
?metastatic from prostate.
Pulmonary embolism.

DR. JAMES B. AYER'S DIAGNOSIS

Malignant lymphoma involving epidural space.

ANATOMICAL DIAGNOSES

Plasma-cell myeloma of fourth thoracic vertebra, with invasion of epidural space and compression of spinal cord.

Pulmonary embolism, massive.
Phlebothrombosis of leg veins, bilateral.
Benign prostatic hypertrophy.

Pathological Discussion

Dr. Taft: At the time of autopsy the patient did have a massive pulmonary embolism, which was bilateral. The source was apparently from the phlebothrombosis of the leg veins that was associated with marked edema of both legs. The prostate was benign both grossly and microscopically. The body of the fourth thoracic vertebra was largely replaced by firm, pale-gray tumor tissue, which extended anteriorly through the periosteum of the vertebra as a rounded, apparently encapsulated mass. It also invaded the epidural space. Many of the bony trabeculae were still present in the vertebral body, however. Microscopically, it was a typical plasma-cell myeloma. There was no apparent involvement of the other vertebras or any of the other bones, either grossly or microscopically. The kidneys showed only minimal nephrosclerosis and congestion. There was no evidence of amyloidosis or of involvement of the tubules with the casts seen in Bence-Jones proteinuria.

Dr. Ayer: Did you find anything low down? We still do not know why the patient had the low spinal-cord symptoms.

Dr. Taft: Nothing was found farther down at the time of autopsy. Microscopically, the spinal cord showed little more than compression effect at the level of the fourth lumbar vertebra.

Dr. Adams: We were perplexed by exactly the same things that disturbed Dr. Ayer. The pain in the legs and low back and the absent knee and ankle jerks suggested a lesion in the upper lumbar or lower thoracic region, whereas the pain in the upper chest indicated a lesion of the second, third or fourth thoracic vertebra. The pyramidal signs could have been due to either lesion. It was probably a technical error not to have visualized both ends of this block before the first exploration. We assumed that we were dealing with multiple lesions and that we could not explain all the symptoms on the lower one. Of course, the lower thoracic region is commonly the site of a false arrest in the myelogram.

Dr. Ayer: Not as false as this as a rule.

Dr. Adams: I still wonder if there was not some pathologic process in the lumbar space to cause these leg pains.

Dr. Ayer: Was the myelographic technic satisfactory?

Dr. Bakay: I did the myelogram, and I was convinced that it was a very uneventful myelogram; the patient was 16 to 20° from the vertical position with his head down, and was then turned in the other direction. Yet the second film was exactly the same as the previous one. Furthermore, the oil moved up and down. The maneuver was repeated twice, which is about as much as an eighty-one-year-old man can stand.

Dr. Ayer: Even myelography may fail sometimes!

The New England
Journal of Medicine

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY
and
THE NEW HAMPSHIRE MEDICAL SOCIETY
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COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

PROGRESS IN THE FIGHT AGAINST YAWS

YAWS is a highly contagious disease that has long been confused with syphilis, and indeed it is due to a closely related organism, *Treponema pertenue*. Particularly prevalent in humid, tropical climates and in rural areas, it is transmitted by human contact, either directly or through clothing or other articles in everyday use by infected persons. Undernourished inhabitants of overpopulated areas are especially susceptible. The lesions of yaws are particularly apt to develop on the feet of those who move about barefoot; this was noted among soldiers in World War II. The disease, which is difficult to recognize before the characteristic lesion appears, apparently is not transmitted congenitally, but healthy infants readily acquire it through contact with infected parents.

Among the chief obstacles confronting physicians and public-health workers in combating yaws is superstition. For some reason there is even a popular belief that a man will not be strong and able to face life successfully unless he has contracted some spectacular form of the disease. As a result, not only have efforts to check its spread been inadequate and archaic, but also children may be deliberately infected from earliest youth and their bodies mutilated by the time they reach the age of twelve.

Encouraging results in the fight against yaws have recently been reported at a conference organized at Bangkok by the World Health Organization in collaboration with the government of Thailand. This conference was attended by outstanding authorities, from all over the world, on this and related diseases. The results of a number of projects conducted by different international teams were presented at the conference. The conviction rapidly grew that yaws could be cured by two or three intramuscular injections of repository penicillin at intervals of a few days. This treatment has proved more effective, less dangerous, cheaper and more manageable than all therapy with orally administered antibiotics, which must be taken for a longer time by the patients, who, despite the serious nature of the disease, often tend to disregard or to forget medical advice very quickly. In addition, the majority of the patients in these regions prefer to undergo injections, sometimes painful ones, rather than swallow other remedies, such as pills, believing perhaps that "something that does not hurt cannot do any good." No tendency of the treponeme of this disease to develop resistance to penicillin was recognized in the course of these studies.

Up to the end of December, 1952, nearly 8,000,000 persons have been examined in Haiti, Indonesia, Thailand and the Philippines in the course of large-scale campaigns against yaws with the assistance of WHO. It has been calculated that the cost of the treatment given, including expenditure for staff and materials, amounts to less than $3 per capita. Thus, only $3 may be considered to be the price

of health and vigor in countries where the community needs an ever-increasing number of workers to improve its lot. This is one of a number of important contributions that WHO is making to improve the health of peoples in many parts of the world where there are not sufficient information and facilities to cope with serious public-health hazards.

"THE BEST IS YET TO BE"

THE matter-of-fact statement that the years over thirty-five constitute the latter half of life has been attributed to Jung, but whether to Carl the psychiatrist or Karl the anatomist is not at this moment clear. Such a precise division of a human life has rather the effect of an anatomic point of view than one relating to the psyche, although, since the anatomist in question died nearly ninety years ago, thirty-five, in his lifetime, was far from representing the midway mark of personal existence. The Biblical three score and ten, for an average life expectancy, was still a good century short of realization.

At best such an interpretation of what might be called middle age implies, not without logic, that life begins rather at birth than at forty, and puts more of a chronologic value on it than one based on its usefulness to its possessor and to society. Such a concept would deny the right of fruit to ripen or of wine to age; it would place the beginning of middle age in the early twenties or even the late teens, if this prime period were allowed to occupy the usual decent percentage of one's life, and would bring it to a close certainly by the time one reached the fifties. The hopeful "Grow old along with me" would have to become practically a spring song, implying twenty years or more of a more or less complacent senescence–complacence depending on various factors.

One such factor would be a reversal, in considering time, of the Doppler principle that as distance lengthens between the receiver of light or sound waves and their source their length appears to be greater than their actual measurement would indicate. This disquieting reversal of a comforting illusion has its compensation in that, although happy days appear to pass too quickly, bad ones, also, do not linger.

The other factor that might disturb the complacence of an early and long senescence would be another reversal, representing the logical converse, applied to the declining years of life, of the theory of the paucity of hypotheses. Whereas in the young a given set of abnormal symptoms is more likely than not to spring from a single pathologic cause, in the elderly, with the various systems of the body undergoing degenerative changes, one is more likely to harbor a number of potential physical catastrophes than a single paltry disease.

How much better it is, on the whole, to adopt the sound principle that productive life, beginning at the close of the purely preparatory years, is what counts, and that "middle age" is that long period through which one passes after the trials of early maturity are over. It implies that the fires of youth, having tempered the molecular structure of the individual, have, by conveniently dying down, allowed it to cool and harden in preparation for a long period of sustained and persistent usefulness.

ARID AREAS IN THE GARDEN OF EDEN

"AND the Lord God said, It is not good that the man should be alone; I will make him an help meet for him (*Genesis* **2**:18)."

The Woman's Auxiliary to the Massachusetts Medical Society came into being in 1948, when physicians as an organization discovered that they needed the help of their wives as an organization. Separately aware of the wisdom and assistance emanating from their homes into the community, a few men had been appraising the value that wives collectively could offer in the expanding areas into which the medical profession had been forced. The threat of socialized medicine quickly crystallized the idea into fact. Thus, the Auxiliary was created from the realization that the Society should not be alone, and it has grown apace with the awareness of its potential for service, with the guidance and at the behest of its appreciative creators.

At the end of five years, it is apparent that thriving district auxiliaries — those contributing to better community health education and services, those building good public relations between the laity

and the medical profession and those exerting positive influence for sound health legislation — are found where medical societies foster immediate and long-range programs within the sphere of Auxiliary activities.

At the recent hearing before the Public Health Committee of the General Court on the three chiropractic bills, 28 Auxiliary members were in attendance and recorded in opposition to passage of these bills. In addition, a statement of opposition from approximately 2000 members was filed with the committee. The President was given her "day in court" to speak in behalf of wives and mothers in a plea to safeguard the health of the citizens; 325 letters to state and district Auxiliary officers and committee chairmen carried the message of the threatening danger. Alerted, Auxiliary members went into action, writing and telephoning their representatives, enlisting the support of their friends and speaking to women's groups and organizations. This is but one instance of the thorough manner in which the Auxiliary can function. However, there are three districts of the Society in which physicians' wives cannot join in concerted effort because there are no active auxiliaries.

What about the areas where the support of an auxiliary has been passive or even denied? Do the respective medical societies agree that "It is not good that the man should be alone?"

REGARDING THE PERMANENTE PLAN

A LETTER published elsewhere in this issue of the *Journal* from Dr. Charles G. Hayden, executive director of Massachusetts Medical Service, calls attention to an editorial in *California Medicine* for January, 1953, written in reply to the editorial "The Permanente Plan's First Ten Years," which appeared in these columns on October 30, 1952. Dr. Hayden suggests the reprinting in full of the California article, but since it is long and space is at a premium an attempt will be made instead to present its salient features.

First, however, it may be desirable to reproduce for the reader's convenience those parts of the *Journal's* editorial of last October on which the writer in *California Medicine* seems to place the greatest emphasis:

> With the cost of medical care rising progressively, with insurance plans such as Blue Cross and Blue Shield forced to increase their premiums while their benefits provide for decreasing proportions of the faster rising costs, and with less and less of the worker's income from wages or salaries available for savings, it is a question whether the supplying to considerable segments of the people of some form of prepayment plan for total medical care can be indefinitely postponed. It is therefore incumbent on the medical profession, as well as other interested parties, to continue to study carefully every apparently successful experiment designed to provide complete medical care of the highest quality to large groups of people at a cost that they can afford and that they can budget. One experiment deserving such scrutiny is the Permanente Plan.

After a condensed history of the plan, taken from the report of its director, Dr. Sidney R. Garfield, published in the Tenth Anniversary Issue of the *Permanente Foundation Medical Bulletin*, the *Journal* goes on to say:

> Details of the plan are worthy of study, for, although Dr. Garfield's presentation might be interpreted as being tinged with enthusiasm and self-interest, the facts of its accomplishment are impressive. It has also been a financial success. In the ten years since the plan was established and while it was developing, participating physicians and professional personnel have been paid $23,500,000, and over $10,000,000 has been paid to non-professional personnel and $1,500,000 to outside physicians and professional people.

After Dr. Garfield's description of the present working of the plan, the *Journal's* editorial closes as follows:

> Certainly this plan is worthy of careful study by physicians throughout the country as one type of program that may not only erect further defenses against the encroachment of socialized medicine but actually provide more and better medical service, at lower cost, and at the same time maintain the dignity of both doctor and patient.

The comments of *California Medicine* in reference to the *Journal's* editorial are in part as follows:

> In California we have long carried out the "careful study" of closed panel plans which the editorialist recommends. We have had the advantage of direct observation, so that our conclusions need not be based wholly upon a report of the medical director of such a plan, which the *New England Journal of Medicine* admits "might be interpreted as being tinged with enthusiasm and self-interest. . . ."
>
> Our study shows closed-panel plans destroy the doctor-patient relationship. This destruction begins with the plan salesman, who must convince the prospective buyer it is to his advantage to break his relation with his personal physician. This is necessary because these plans offer no provision for indemnification of the patient who prefers his own doctor to the plan doctors . . . .

Another destroyer of the doctor-patient relationship is the rapid turnover of Permanente doctors,

according to *California Medicine*, which finds also that closed-panel plans rob the patient of his freedom; important, too, in illustrating the unfair competition represented by such plans is the statement that Permanente doctors solicit their patients whereas doctors outside the plan may not do so.

Revealing, too, is the following quotation from *California Medicine's* editorial:

> And now, specifically as to Permanente. Who and what is Permanente? In California, when we have difficulty with Permanente, we start with the doctor or doctors then acting as medical directors and end up talking to Mr. Henry Kaiser. We have no technical proof that Permanente is the practice of medicine by a layman. But we inevitably end up talking to — or, more accurately, being talked to and often threatened by — Mr. Kaiser. Our medically trained minds cannot follow Permanente's intricate intercorporate entanglements, rental arrangements, partnership, interorganizational contracts and pooled personnel and purchasing arrangements. But we know that what Mr. Kaiser says will happen in Permanente usually happens.
>
> Here, then, in our opinion, is the pattern for lay practice, control and direction of a profession. We need not argue the public interest factors in this condition. They have long since been decided and repeatedly reaffirmed by the courts. How many profit-minded laymen will see in the "Permanente idea" the opportunity to "reverse the usual economics of medicine" for themselves? And what will they do with it? Whom will they exploit? And to whom will they be answerable?

There is always risk of creating misunderstanding in lifting passages from their context and using them as representative of the intent of their writer. In this case, however, the attempt has been made to present, in limited space, *California Medicine's* greatest objections to the Permanente Plan.

The *New England Journal of Medicine* holds no brief for the Permanente Plan, which, despite its name, may be thoroughly discredited ten years from now, nor has it the slightest inclination to quarrel with *California Medicine* for opposing it. It continues to advocate the open-minded study of any plan of medical practice that may contribute the greatest good to the greatest number of persons and permit the equable distribution of medical care to advance in as straight lines as possible. This, it may be hoped, is the long-term view held by all physicians, despite their concern over the defects that may be apparent in any immediate situation. And in this way, by the gradual improvement and extension of voluntary plans, the socialization of medicine may be avoided.

The statement in *California Medicine* that the *Journal's* editorial "cites closed panel medical plans in general, and the 'Permanente idea' in particular as 'worthy of careful study by physicians. . . .' " remains unclear, since closed-panel medical plans in general were not mentioned.

By the recent influx of reports from all sections of the Union, it is pretty conclusively shown that lunacy is not confined to New England.

Boston M. & S. J., *April 27, 1853*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BURKE — Michael F. Burke, M.D., of Natick, died on April 9. He was in his eighty-first year.

Dr. Burke received his degree from Harvard Medical School in 1896. He was medical examiner of the eighth Middlesex District and was a member of the staffs of the Carney, Newton-Wellesley, Glover Memorial, Framingham Union and Lawrence Memorial hospitals. He was a fellow of the American College of Surgeons and American Medical Association.

He is survived by a daughter, three sons and nine grandchildren.

LUCE — Dean S. Luce, M.D., of Canton, died on April 9, He was in his seventy-eighth year.

Dr. Luce received his degree from Harvard Medical School in 1904. He was senior staff member of Norwood Hospital, a member of the staff of Milton Hospital, editor-in-chief of *Norfolk Medical News*, a former president of Norfolk District Medical Society and a member of the Council of the Massachusetts Medical Society and was a fellow of the American Medical Association.

He is survived by his widow, a daughter and a brother.

CORRESPONDENCE

ANTIFLUORIDATION

To the Editor: The obsession of the opponents of fluoridation makes the problem of dental decay particularly serious at present.

Articles appearing in the western part of the State say that fluoride causes cancer, kidney and heart disease, physical and mental deterioration, sterility, stillbirths, fear, greed and mass hate, is mass medication and communistic, eats out pumps and pipes, is being pushed down people's throats and is good for nothing but killing rats. People leap to the conclusion, after reading such material, that partial destruction of many parts of the organism will result or that life will be extinguished by the ingestion of fluoride despite the fact that epidemiologic studies by eminent scientific professional researchers, have proved these statements to be near-idiocy.

Now or never, the medical and dental professions must protect the public from oratorical activities and influences that are creating erroneous impressions about fluoridation. They must preserve the records, publicize the documented facts and reveal the scientific research of all public-health organizations, which are the targets of attack by ignorant persons. The people of the Commonwealth are dealing with

a paradox; good judgment is at stake and also the health of the children of the State, for making teeth more resistant to decay affects general health and is of equal concern to both the medical and dental profession, as well as to all parents.

CLARENCE W. WILDMAN, D.M.D.
Fluoride Committee
Council on Dental Health
Massachusetts Dental Society
North Adams, Massachusetts

EFFECTS OF FLUORIDATION

To the Editor: In writing in reply to an article by John W. Knutson, in the May 8 issue of the *Journal*, entitled "The Case for Water Fluoridation," I wish to refer to a reprint of an article I wrote on this subject in 1949, entitled "Toxic Level of Fluorine in Water Supplies" (*Am. J. Dis. Child.* **78**: 72-76, 1949). I am unable to explain the work of Dean and McKay, but I know that mottling of the teeth occurs in this area where fluorine is present to one part per million. I have never made any study regarding dental caries, but we have a great deal of it and several dentists in this area believe that it is more severe than average. I also refer you to the work of H. V. Smith at the University of Arizona regarding experimental production of dental fluorosis in which he did not believe that fluoridation decreased dental caries.

In my opinion the United States Public Health Service is on the wrong track regarding fluoridation of water supplies, and I think that before any measure is adopted more work should be done in the endemic areas of dental fluorosis, preferably by physicians or dentists and not by Public Health Service personnel.

D. C. BADGER, M.D.
Hobbs, New Mexico

MASSACHUSETTS FEDERATION OF NURSING HOMES

To the Editor: In the last ten years, especially since 1948, there has been a revolutionary change in the nursing-home profession in Massachusetts. In 1948, the supervision of nursing homes came into the domain of the Massachusetts Department of Public Health. Stringent regulations, subtle pressures and skillful appeal to pride are producing nursing homes that are on their way to a high level of standards. Today, the 500 nursing homes in this state are rapidly becoming adjuncts to the overcrowded hospitals. In this metamorphosis due credit must be given to the Massachusetts Federation of Nursing Homes.

This organization, which was founded in 1949, today includes about 200 of the better nursing homes in the Commonwealth. The organization is guided by a code of ethics. An applicant is admitted only after complying with a standard procedure consisting of references from three physicians, reports from the local welfare department and Massachusetts Department of Public Health, and an examination of the applicants by an inspection team. Frequent educational conferences and panels have been introduced and sponsored by the Massachusetts Federation of Nursing Homes with social-service workers and state officials; lectures on geriatrics and psychiatry have been given by medical specialists.

The Federation is proud of its accomplishments in the short time it has been in existence. Recently it supported two of its member homes in a court suit against the Tax Department of Massachusetts concerning the meal tax on patients in nursing homes and hospitals — and won a decision. It has been able to obtain professional malpractice insurance for its members. It has inaugurated an official publication — the *Journal of the Massachusetts Federation of Nursing Homes*. It has originated a nursing-home day. It is a charter member of the American Association of Nursing Homes.

The Federation looks forward to the future with confidence. It knows that it can police its own members. It is constantly striving for higher standards. It hopes to develop a warm association with the Massachusetts Medical Society and the Massachusetts Hospital Association.

RAYMOND M. DORNE, M.D.
Chairman, Committee of Ethics and Standards
Massachusetts Federation of Nursing Homes
Stoneham, Massachusetts

QUASI-QUIBBLES

To the Editor: Carrying on the quasi-quibbles so entertainingly set forth in the "Correspondence" column of the March 19 issue of the *Journal*, I am led to wonder whether those playing with the thought that the Medical Society of London's copy of Dr. Douglas's "Appendix" may now be unique are aware that the *Index-catalogue* (first series) of the Armed Forces Medical Library lists a copy for that library. Of course, there may be knowledge that that copy is lost, or even the not entirely riotous thought that it is *probably* lost.

As you and Sir Zachary Cope certainly know, Douglas started out (the *History*, 1726, p. 86) with the more modest claim that, barring accidents, Cheselden seldom took more than a minute (sometimes less) for the operation (though this was before the technic was perfected, of course). Any quibbling over this issue one might say, therefore, was started by the Scotch-born Dr. Douglas.

W. B. McDANIEL, II
Librarian, College of Physicians of Philadelphia
Philadelphia, Pennsylvania

CALIFORNIA MEDICINE AND THE PERMANENTE PLAN

To the Editor: If it is the policy of the *Journal* to air both sides of controversial questions, I should like to call your attention to an editorial in the January, 1953, issue of *California Medicine*, the official journal of the California Medical Association, which is sent free to all delegates to the American Medical Association. This editorial appears to be a response to your October 30, 1952, editorial concerning the controversial Permanente Hospital and medical plan on the West Coast.

According to *California Medicine*, Permanente's combination of closed-panel practice and prepayment is nothing more nor less than a dressed-up version of what used to be known as "lodge practice." This is an interesting observation because, if true, its implications involve not only Permanente but also a number of lay-sponsored closed-panel plans, including the controversial Health Insurance Plan of Greater New York about which a good deal was recently published in the *Journal of the American Medical Association*.

It seems to me that in fairness to your readers you should reprint the entire editorial from *California Medicine*. Only in that way will they get the other side of this important subject.

CHARLES G. HAYDEN, M.D.
Executive Director, Massachusetts Medical Service
Boston

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Ego Development and the Personality Disorders: A developmental approach to psychopathology. By David P. Ausubel, M.D., Ph.D., Bureau of Research and Service, College of Education, University of Illinois, Urbana. 8°, cloth, 564 pp. New York: Grune and Stratton, 1952. $10.00.

Childhood Experience and Personal Destiny. By William V. Silverberg, M.D., clinical professor of psychiatry, New York Medical College. 8°, cloth, 289 pp. New York: Springer Publishing Company, Incorporated, 1952. $4.50.

The Love and Fear of Flying. By Douglas D. Bond, M.D., professor of psychiatry and head, Department of Psychiatry, Western Reserve University School of Medicine. With a preface by General H. Doolittle. 8°, cloth, 190 pp. New York: International Universities Press, Incorporated, 1952. $3.25.

Human Locomotion and Body Form: A study of gravity and man. By Dudley J. Morton, M.D. With the collaboration of Dudley D. Fuller, associate professor, Department of Mechanical Engineering, Columbia University. 8°, cloth, 285 pp., with 82 illustrations. Baltimore: Williams and Wilkins, 1952. $5.00.

Psychoanalytic Explorations in Art. By Ernst Kris, Yale University School of Medicine, Child Study Center. 8°, cloth, 358 pp., with 79 illustrations. New York: International Universities Press, Incorporated, 1952. $7.50.

Correlative Cardiology: An integration of cardiac function and the management of cardiac disease. By Carl F. Shaffer, M.D., associate professor of clinical medicine, Baylor University College of Medicine; and Don W. Chapman, M.D., associate professor of medicine, Baylor University College of Medicine. 8°, cloth, 525 pp., with illustrations. Philadelphia: W. B. Saunders Company, 1952. $9.50.

NOTICES

ANNOUNCEMENT

Dr. Schoul Levison announces the removal of his office from 117 Bay State Road to 483 Beacon Street, for the practice of neurology and psychiatry.

PHI CHI FRATERNITY

The annual lecture of Delta Chapter of Phi Chi Medical Fraternity will be presented in Stearns Auditorium, New England Center Hospital, on April 29, at 8 p.m. Stanley J. G. Nowak, M.D., surgeon-in-chief, Mount Auburn Hospital, will speak on the subject "Peripheral Arterial Disease, with a Description of a New Syndrome."

All physicians and medical students cordially invited.

NEW ENGLAND CENTER HOSPITAL HOUSE OFFICERS' ASSOCIATION

The following program will be presented in the Evening Lecture Series of the House Officers' Association of New England Center Hospital in the Stearns Auditorium of the Hospital on Friday, May 1, at 7 p.m.:

Practical Considerations in the Management of Diabetes. Dr. Garfield G. Duncan, clinical professor of medicine, Jefferson Medical College, and director of the medical divisions, Pennsylvania Hospital and Benjamin Franklin Clinic.

Drs. Priscilla White and Joseph Rosenthal will lead the discussion.

All interested persons are invited to attend.

NEW ENGLAND CARDIOVASCULAR SOCIETY

The Henry Jackson Lecture will be presented in the Dorothy Quincy Suite, John Hancock Hall, 180 Berkeley Street, Boston, on Monday, May 11, at 8:15 p.m., under the auspices of the New England Cardiovascular Society. Elliot V. Newman, M.D., a professor of experimental medicine and chief, Laboratories of Clinical Physiology, Vanderbilt University School of Medicine, will speak on the subject "Metabolic Adjustments to Normal and Disturbed Circulation in Man."

A short business meeting will precede the lecture.

Interested physicians, medical students and members of the New England Postgraduate Assembly are cordially invited to attend.

AMERICAN PROCTOLOGIC SOCIETY

The American Proctologic Society will hold its fifty-second annual meeting at the Hotel Statler, Boston, June 10 to 13 inclusive. Further information may be obtained from Dr. E. Parker Hayden, 270 Commonwealth Avenue, Boston.

AMERICAN THERAPEUTIC SOCIETY

The annual meeting of the American Therapeutic Society will be held in the Hotel Biltmore, New York City, May 28-31.

Outstanding in the program is a Symposium on Tobacco (Dr. Arthur C. DeGraff, New York City, moderator), which includes the following papers:

The Allergic Response to Tobacco. Dr. W. C. Spain, New York City.

The Influence of Smoking Upon the Gastrointestinal Tract. Dr. Robert C. Batterman, New York City.

Evaluation of the Effects of Tobacco Smoking on the Central Nervous System, Organic or Psychiatric. Dr. H. Randolph Unsworth, New Orleans.

Vascular Responses to Tobacco. Dr. A. Wilbur Duryee, New York City.

The Effects of Smoking of Nicotine on the Cardiovascular System of Normal Persons and Patients with Hypertension. Dr. Grace Roth, Mayo Clinic.

The Pharmacology of Tobacco. Dr. Harvey B. Haag, Richmond.

Role of Tobacco in Pulmonary Cancer. Dr. Ernest L. Wynder, Memorial Hospital, New York City.

In addition the program includes round-table discussions and symposiums on Recent Advances in Medicine (Dr. O. P. J. Falk, St. Louis, moderator) and Recent Advances in Surgery (Dr. W. Wayne Babcock, Philadelphia, moderator). An entire day will be devoted to new items in the therapeutic armamentarium.

Guests are welcome to attend the scientific sessions.

SOCIETY MEETINGS AND CONFERENCES

April 29. Phi Chi Fraternity. Notice above.

April 29 and October 28. New England Obstetrical and Gynecological Society. Page 868, issue of November 27.

May 1. New England Center Hospital House Officers' Association. Notice above.

May 2. When Is the Treatment of Mitral Stenosis Surgical? Drs. Laurence B. Ellis and Dwight E. Harken. Mount Auburn Hospital, Cambridge. 10:05 a.m.

May 4. Massachusetts Department of Mental Health. Postgraduate Seminar in Neurology and Psychiatry. Page 540, issue of October 2.

May 6. Cutter Lecture on Preventive Medicine. Page 663, issue of April 9.

May 6-8. American Association of Genito-Urinary Surgeons. Page 709, issue of April 16.

May 7-9. American Goiter Association. Page 480, issue of March 12.

May 11. New England Cardiovascular Society. Notice above.

May 11-13. Aero Medical Association. Page 526, issue of March 19.

May 18-22. National Tuberculosis Association. Page 664, issue of April 9.

May 19-21. Massachusetts Medical Society. Hotel Statler, Boston.

May 20. Massachusetts School Physicians' Association. Page 663, issue of April 9.

May 25-31. First World Congress on Fertility and Sterility. Page 1001, issue of December 18.

May 28-31. American Therapeutic Society. Notice above.

May 30 and 31. Society for Investigative Dermatology, Inc. Page 570, issue of March 26.

June 7-9. American College of Cardiology. Page 395, issue of February 26.

June 10-13. American Proctologic Society. Notice above.

June 26-28. American Academy of Dental Medicine. Page 664, issue of April 9.

June 28-July 2. American Society of X-Ray Technicians. Page 480, issue of March 12.

July 8 and 9. Seventh Annual Rocky Mountain Cancer Conference. Page 644, issue of April 9.

August 18-21. Third International Congress of Electroencephalography and Clinical Neurophysiology. Page 707, issue of April 16.

District Medical Societies

ESSEX NORTH

May 13. Andover Country Club, Shawsheen.

WORCESTER

May 6. Annual Meeting. Sheraton Hotel. Dr. Louis H. Bauer, President, American Medical Association.

Calendar of Boston District for the Week Beginning Thursday, April 30

Thursday, April 30

*8:30-10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.

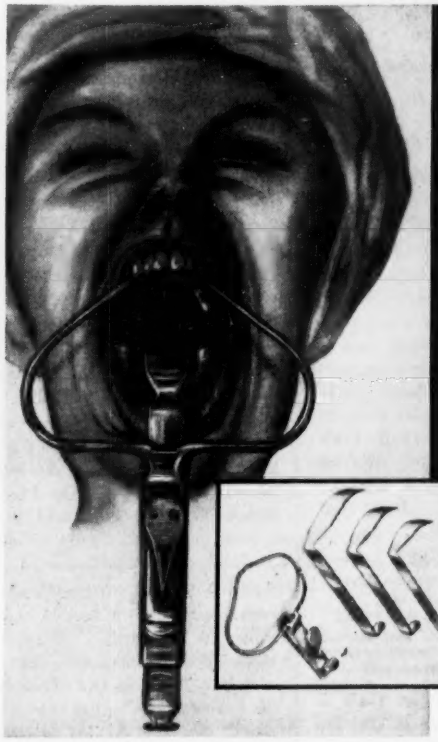
*9:00-10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.

*11:00 a.m.-12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.

*12:00 m.-1:00 p.m. Experiences with Valvular Heart Disease and Cardiac Surgery at the Veterans' Hospital. Dr. David Littmann. Stearns Auditorium, New England Center Hospital.

*5:00-6:00 p.m. Surgical Division Meeting. Mount Auburn Hospital, Cambridge.

(*Notices concluded on page xiii*)



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WANTED — Diplomate of American Board of Pathology to act as military substitute for pathologist expecting to be called in service. Address A227, *New Eng. J. Med.* 16-4t

VACATION WITH PAY — Physician and wife for exclusive New England hotel, July and August. Must undertake at least 2 weeks. Address A228, *New Eng. J. Med.* 16-3t

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WANTED — Board-qualified obstetrician-gynecologist, 36 years or under, for The Walla Walla Clinic, 55 Tietan Street, Walla Walla, Washington. B245-14-6t

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SURGEON, with Part I of Board, desires paying residency or junior staff position, hospital in East, July 1, 1953 — January 1, 1954. Excellent recommendations; 5 years' excellent residency training. Awaiting new appointment January 1, 1954. Address A231, *New Eng. J. Med.* 17-tf

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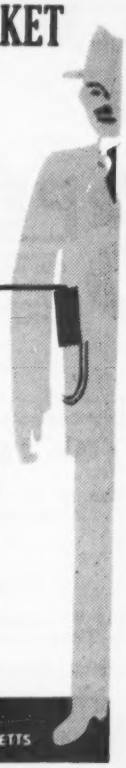

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NOTICES (*Concluded from page 746*)

FRIDAY, MAY 1

*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.

*10:00 a.m.–1:00 p.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.

*10:30–11:15 a.m. Diabetes Lecture. Dr. Elliott Joslin. New England Deaconess Hospital.

*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.

*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.

*4:00–10.00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

*7:00 p.m. New England Center Hospital House Officers' Association. Dr. Garfield G. Duncan. Stearns Auditorium, New England Center Hospital.

SATURDAY, MAY 2

*9:00 a.m. Proctology Clinic. Peter Bent Brigham Hospital.

*9:00 a.m. Alcoholism Clinic. Peter Bent Brigham Hospital.

10:05 a.m. When Is the Treatment of Mitral Stenosis Surgical? Drs. Laurence B. Ellis and Dwight E. Harken. Mount Auburn Hospital, Cambridge.

*11:00 a.m.–12:00 m. Blood Clinic. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, MAY 4

*8:00–9:00 a.m. Combined Medical and Surgical Rounds for Diabetic Surgery Cases. New England Deaconess Hospital.

*8:30–9:30 a.m. Clinic by entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.

12:00 m. Clinicopathological Conference (Boston Floating Hospital). Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.

*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

*2:00–8:30 p.m. Postgraduate Seminar in Neurology and Psychiatry. Metropolitan State Hospital, Waltham.

*7:00–9:00 p.m. Anesthesia Teaching Conference. Stearns Auditorium, New England Center Hospital.

TUESDAY, MAY 5

*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.

*12:00 m.–1:00 p.m. Regular Grand Rounds of the Pediatric Department. Dowling Amphitheater, Boston City Hospital.

*12:00 m.–1:00 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

*12:15–1:15 p.m. X-ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.

5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.

*5:00–6:00 p.m. Service Meeting followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.

WEDNESDAY, MAY 6

*11:00 a.m.–12:00 m. Pediatric Grand Rounds. (Children's Medical Center.) Jimmy Fund Building, 25 Binney Street.

*12:00 m. Boston State Hospital Psychiatric Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.

*12:00 m.–1:00 p.m. Medical Conference. (Children's Medical Center.) Jimmy Fund Building, 25 Binney Street.

12:30 p.m. Weekly Pathological Meeting. Joslin Amphitheater, New England Deaconess Hospital.

12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.

*2:00–3:00 p.m. Pediatric Conference for Practitioners. (Children's Medical Center.) Jimmy Fund Building, 25 Binney Street.

*4:00 p.m. Thoracic Conference. Held by Overholt Clinic. Harris Hall, New England Deaconess Hospital.

*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.

*Open to the medical profession.

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Apr. 23, 1953

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